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IN THIS ISSUE

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DRUG EVALUATIONS

by the Council on Pharmacy and Chemistry of the American Medical Association

The following monographs and supplemental statements on drugs have been authorized by the Council on Pharmacy and Chemistry of the American Medical Association for publication and inclusion in *New and Nonofficial Remedies*. They are based upon the evaluation of available scientific data and reports of investigations. In order to make the material even more valuable, dosage forms and preparations of individual drugs have been added to the monographs. These dosage forms and preparations were not taken from material published in the *Journal of the American Medical Association* by the Council on Pharmacy and Chemistry; rather, they were obtained from such manufacturers' brochures, news releases, etc., which were available to us at the time of publication. An attempt has been made to make the list of dosage forms as complete as possible. However, no guarantee can be made that the list of preparations is complete and it is suggested that hospital pharmacists consult manufacturers' releases for additional dosage forms and preparations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of THE BULLETIN include those published in the *Journal* to October 1, 1956.

INDEX TO EVALUATED DRUGS, THIS ISSUE

INDEX TO EVALUATED DRUGS PUBLISHED IN THE MAY-JUNE, JULY-AUGUST, AND SEPTEMBER-OCTOBER ISSUES OF THE BULLETIN

Acetazolamide — Diamox® Additional Uses Of

The Council has evaluated the use of acetazolamide for the treatment of toxemia and edema of pregnancy, premenstrual tension, obesity, and drug-induced edema. This diuretic agent previously has been found useful for the management of cardiac edema, epilepsy, and glaucoma. On the basis of currently available evidence, the Council concluded that its oral administration to patients with toxemia and edema of pregnancy often will provide relief from the fluid retention that accompanies or characterizes mild preeclampsia of the third trimester. The drug is also useful for the treatment of the discomforts of premenstrual tension associated with fluid and electrolyte retention. Acetazolamide has been employed as an adjunct to dietary and other therapeutic measures for the management of simple obesity and excessive weight gain during pregnancy; preliminary results indicate a salutary effect in some patients. The drug also may be administered with phenylbutazone or cortisone to control the edema induced by these agents. The possibility of untoward effects from long-term use has not been assessed.

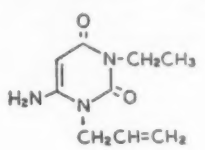
Acetazolamide is administered orally for all of the foregoing indications. Doses of 0.25 gm. daily are usual for the treatment of toxemia and edema of pregnancy. For premenstrual tension accompanied by fluid retention, doses of 0.25 gm. per day beginning 6 to 10 days prior to onset of menstruation or at the onset of symptoms have been employed; however, doses considerably lower than this may be adequate. The average dose for the adjunctive management of obesity is 0.25 gm. each day. When control of drug-induced edema is desired, doses of 0.25 gm. twice weekly may be tried.

The Council voted to amend New and Nonofficial Remedies to describe these additional uses of acetazolamide.

Lederle Laboratories Division, American Cyanamid Company, cooperated by furnishing scientific data to aid in the evaluation of these additional uses of acetazolamide.
—*J. Am. Med. Assoc.* *162*:207 (Sept. 15) 1956.

Aminometradine — Mictine®

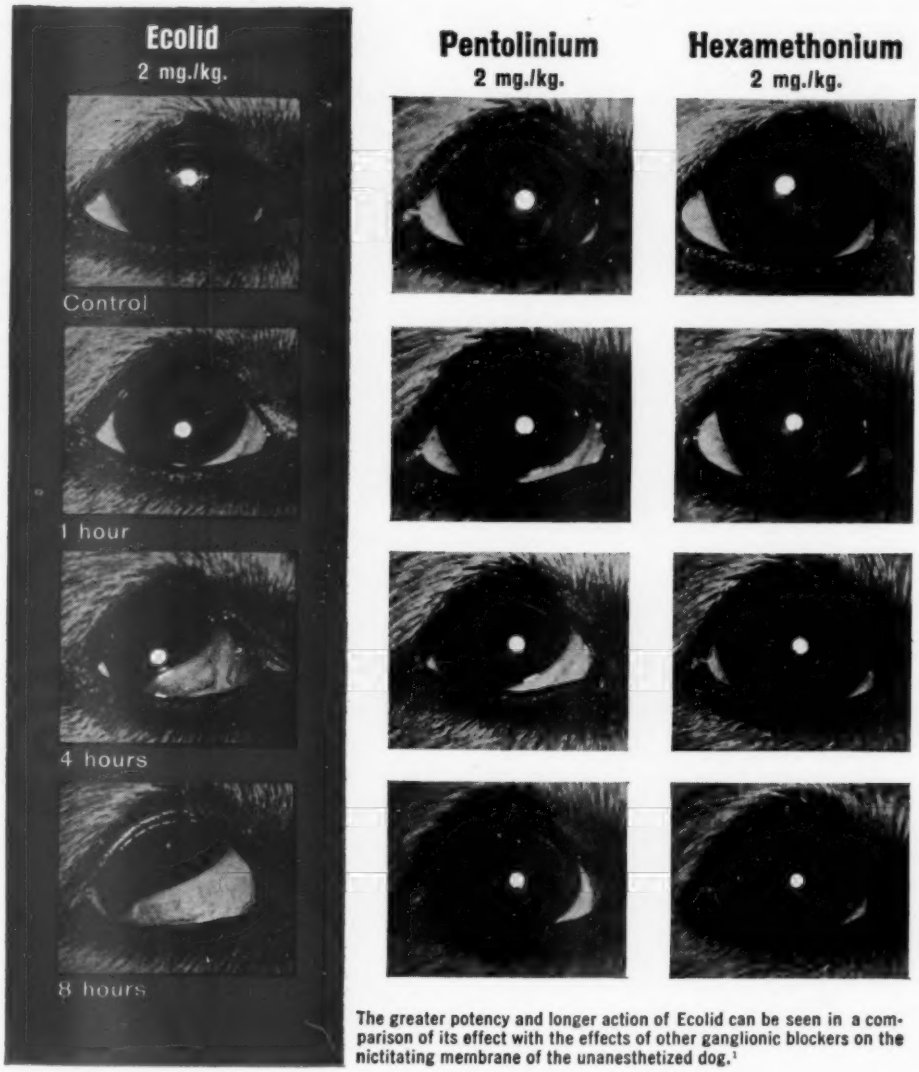
AMINOMETRADINE is 1-allyl-3-ethyl-6-aminotetrahydropyrimidinedione.—The structural formula of aminometradine may be represented as follows:



Actions and Uses

Aminometradine, a synthetic uracil derivative, produces an increased flow of urine after oral administration. Its precise mode of action is not clear but is believed to be that of inhibiting the reabsorption of sodium ions by the renal tubule; potassium excretion is slight and variable. The drug does not affect carbonic anhydrase or succinic dehydrogenase and appears to have no significant effects on renal blood flow or glomerular filtration rate. In contrast to acetazolamide or the mercurial diuretics, aminometradine does not

When less potent antihypertensives fail . . .



The greater potency and longer action of Ecolid can be seen in a comparison of its effect with the effects of other ganglionic blockers on the nictitating membrane of the unanesthetized dog.[1]

Ecolid®
chloride
(chlorisondamine chloride CIBA)

CIBA
SUMMIT, N. J.

Clinically, reduction in blood pressure instituted with Ecolid was more effective, more consistent and more prolonged at a lower oral dosage than with other ganglionic blockers, including hexamethonium and pentolinium.[2-4] Patients preferred Ecolid to hexamethonium "... for reasons varying from relief of constipation to need to take fewer tablets a day."[4] Ecolid is recommended in moderate, severe, even malignant hypertension.

For complete information on dosage recommendations, management of side effects and precautions, please write Medical Service Division for booklet entitled *"Ecolid — A New Ganglionic Blocker for Hypertension."*

1. Plummer, A. J., Trapold, J. H., Schneider, J. A., Maxwell, R. A., and Earl, A. E.: J. Pharmacol. & Exper. Therap. 115:172 (Oct.) 1955. 2. Grimson, K. S.: J.A.M.A. 158:359 (June 4) 1955. 3. Smith, J. R., and Hoobler, S. W.: Univ. Michigan M. Bull. 22:51 (Feb.) 1956. 4. Grimson, K. S., Tarazi, A. K., and Frazer, J. W., Jr.: Circulation 11:733 (May) 1955.

Supplied: Ecolid Tablets (Rotocotes), 25 mg. (ivory) and 50 mg. (pink).

ROTOCOTES T.M. (dry-compressed, coated tablets CIBA) 2/2324M

alter urinary pH nor does it cause significant changes in the systemic acid-base balance. Like acetazolamide and the xanthines, however, the drug has only minimal diuretic effects in normal, nonedematous individuals.

Aminometradine is an effective agent for the treatment of edema in patients with congestive heart failure. In mild to moderate cases, the drug may be used to initiate diuresis and subsequently to maintain an edema-free state. It is sometimes effective in producing diuresis in these patients when the organic mercurials fail. Conversely, other patients may respond well to the mercurials but not to aminometradine. There is suggestive evidence that the drug is most effective in patients with elevated serum sodium levels; its judicious use has sometimes reduced or eliminated entirely the need for mercurial diuretics.

Patients with severe cardiac decompensation and attending ascites, pulmonary edema, orthopnea, or dyspnea usually do not respond well to initial therapy with aminometradine. In such cases, rapid mobilization of edema fluid can best be achieved by paracentesis and/or administration of the mercurials. Once the acute congestive failure has been compensated, however, it is frequently possible to keep such patients in an edema-free state by the administration of maintenance doses of aminometradine. Regardless of the severity of congestive heart failure, the diuretic should be administered as an adjunct to and not as a substitute for other forms of therapy such as cardiac glycosides and a low-sodium diet.

Although the most satisfactory results with aminometradine have occurred in patients with congestive heart failure, the drug has also been of value in certain other conditions characterized by edema. Thus, in some patients with cirrhosis of the liver or the nephrotic syndrome, its administration may produce a moderate diuresis. In some patients with cirrhosis, this may be sufficient to eliminate or at least curtail the need for mercurials. There is also some preliminary evidence that aminometradine may be useful for the treatment of edema associated with the administration of adrenal cortical steroids and phenylbutazone. Sufficient valid evidence is lacking, however, of the drug's usefulness in toxemia of pregnancy or premenstrual tension.

Aminometradine has not so far been reported as causing serious toxic effects, and there are no known contraindications to its use. Although its metabolic fate is imperfectly understood, it appears to be a relatively safe agent for use in the presence of severe cardiac, hepatic, or renal damage. Minor side-effects are common; nausea and vomiting occur in about 20 to 30% of the patients to whom it is administered. Rarely, these may be of sufficient severity to necessitate discontinuation of therapy or reduction of dosage below effective levels. Other side-effects such as anorexia, headache, and diarrhea are infrequent and mild.

Dosage

Aminometradine is administered orally. Dosage must be determined individually according to the severity of the edema. For the initiation of diuresis or for maintenance therapy in adults and children, the daily requirement ranges from 0.2 to 0.8 gm. In an effort to minimize gastric disturbances, this amount is administered on an interrupted dosage schedule. This may be accomplished either by administration of 0.2 to 0.8 gm. every day in divided doses during meals or by administration of this amount in divided dosage during meals for three consecutive days and then complete omission on the following four days.

Preparations for use as stated for the foregoing drug are marketed under the following name: Mictine.

G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of aminometradine.

—*J. Am. Med. Assoc.* 162:116 (Sept. 8) 1956.

Preparations

Tablets Aminometradine (Mictine) 0.2 Gm.

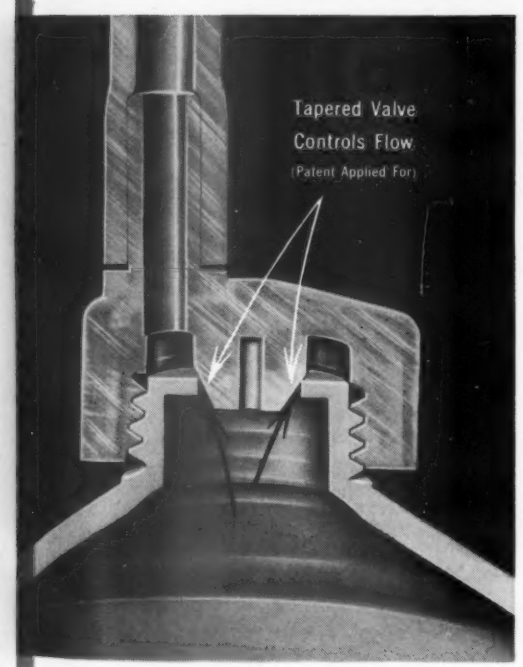
Antivenin (Crotalidae) Polyvalent

ANTIVENIN (CROTALIDAE) POLYVALENT is North and South American Antisnakebite Serum.—An antitoxin obtained from the serum of horses that have been immunized with the venom of four crotaline snakes (C. atrox, C. adamanteus, C. durissus terrificus, and B. atrox). The antivenin, dried by vacuum dehydration from the frozen state, retains its potency for at least five years and is readily soluble in water for injection. It is standardized by its ability to neutralize the toxic action of a standard venom by concomitant intravenous injection into mice.

Actions and Uses

Antivenin (crotalidae) polyvalent contains protective substances against the venom of certain crotaline snakes (pit vipers) as demonstrated by its ability to neutralize the toxic effects of supralethal doses of venom injected into mice. Crotaline venoms against which it is theoretically protective in man include those of most of the common pit vipers of North and South America, such as the rattlesnake, moccasin, copperhead, fer-de-lance, tropical rattler, cantil, and bushmaster. Because of known variations in venom antigenicity among various species of the family crotalidae, it is not known whether the serum contains protective substances against the venoms of all pit vipers. Since it would be almost impossible to obtain extensive clinical evidence with the antivenin in persons bitten by snakes, and since the serum is lifesaving in mice, it is a proper presumption that it will be beneficial in the treatment of human victims of crotaline snake bite. The drug is of no value for the neutralization of venom following bites inflicted by noncrotaline snakes such as the American coral snake, the true vipers, including the puff adder, the cobras, and the mamba, or any of the venomous spiders or scorpions.

While antivenin (crotalidae) polyvalent is considered useful in the treatment of envenomization, its administration ordinarily should follow the use of well-established emergency first-aid procedures. These include the immediate application of a tourniquet, not too tightly applied when an extremity is involved, and incision and suction at the site of the bite. When a tourniquet is used, periodic release is necessary to avoid gangrene. When such emergency measures have been delayed too long to make them useful, antivenin should be considered the initial method of therapy. Chemical freezing, as with ethyl chloride, or prolonged exposure to cold, as by immersion in ice water, should be avoided because of the likelihood that this enhances the hypoxic condition caused by the hemorrhagic and proteolytic snake venoms. In cases of potentially fatal bites by large snakes, experiments with animals indicate that life can always be saved at the cost of a limb by quick application of a tight tourniquet and subsequent amputation.



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These tests produced a 6 inch rectal tube sufficiently stiff for ease of insertion yet smooth and pliant to the patient. Possible damage to the mucosa is prevented by the soft round tip.

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Clinical studies show that for routine enemas, the time-proved phosphate solutions are superior for both cleansing effects as well as cost of administering.[1]

Packed in easy-to-handle 24 to a case, 4½ oz. units.

1. Kehlmann, W. H., Time Study On New Enema Technic, Modern Hospital, May 1955.

*TM

SINCE CUTTER 1897

Enemol

CUTTER LABORATORIES
Berkeley, California

Dosage

Antivenin (crotalidae) polyvalent is administered subcutaneously, intramuscularly, or intravenously in doses of 10 to 50 cc. of reconstituted serum, depending on severity of symptoms, lapse of time after bite, size of snake, and size of patient (the smaller the body of the victim in relation to the size of the snake, the larger the dose required). The freeze-dried serum should be reconstituted immediately prior to use. Preliminary intradermal and conjunctival tests for sensitivity to horse serum should be carried out before administration of the antivenin if there is a history of allergy. If desensitization is not required, the estimated dose is administered by separate injections, not to exceed 10 cc. at any site. If the victim is treated within two hours, a small quantity of the serum may be injected around the wound (except for bites on the digits); otherwise the entire dose should be administered higher on the bitten limb. The initial dose is the most important one, since viper venoms rapidly break down blood vessels and thus impede systemic absorption of the serum; therefore, the initial dose should be large enough to saturate the system and overwhelm the toxin. If symptoms such as swelling or pain persist or recur, additional doses may be injected every 30 minutes to 2 hours, as necessary. Although the serum frequently may be administered by laymen as an emergency procedure, it should not be given intravenously except by a physician and then only in grave cases. All patients should be hospitalized if possible, and blood typing for transfusion should be performed as soon as possible because alteration of the blood pattern by the venom soon may make accurate cross-matching impossible.

Preparations for use as stated for the foregoing drug are marketed under the following name: Antivenin (Crotalidae) Polyvalent.

Wyeth Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of antivenin (crotalidae) polyvalent.

—*J. Am. Med. Assoc.* *161*:138 (Aug. 4) 1956.

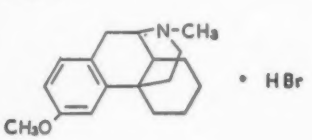
Preparations

Antivenin (Crotalidae) Polyvalent (North and South American Antisnakebite Serum) combination package containing one vial Antivenin, one syringe of Water for Injection U.S.P. (with preservative), one vial of Iodine Solution N.F., one vial of Normal Horse Serum 1:10 dilution, and one sterile needle.

Dextromethorphan Hydrobromide

Romilar® Hydrobromide

DEXTROMETHORPHAN HYDROBROMIDE is *d*-3 methoxy-N-methylmorphinan hydrobromide.—The structural formula of dextromethorphan hydrobromide may be represented as follows:



Actions and Uses

Dextromethorphan hydrobromide, a synthetic morphine derivative, is employed exclusively as an antitussive agent. Unlike codeine, dihydrocodeinone, and many of the other opium alkaloids used for this purpose, it exhibits little or no central depressant activity and does not produce analgesia. In addition, the drug appears to have no addicting effects, even after prolonged use in rather high doses. Its toxicity is low; side-effects reported to date have been slight, and there is some doubt that these can be attributed to the drug at all. The amount of bromine present in therapeutic doses is of no clinical significance.

As with any antitussive drug, it is extremely difficult to obtain unbiased clinical data on effectiveness. With agents that have concomitant sedative actions, the possibility exists that patients become less conscious of and, hence, less bothered by cough although the actual frequency and intensity of cough is little affected. Dextromethorphan, however, has been subjected to well-controlled clinical evaluation. In a series of patients with severe chronic cough of varied etiology, dextromethorphan hydrobromide, codeine, and a placebo were administered under double-blind conditions; cough was rated numerically and recorded four times daily. The data obtained from a large number of such observations were subjected to a statistical analysis of variance. Only after the data had been thus analyzed was the identity of the medicaments revealed. These studies demonstrated that both dextromethorphan and codeine produced a definite and significantly greater diminution in cough than did the placebo. Thus, dextromethorphan hydrobromide compares favorably with the other antitussives used in clinical practice. Its activity in this respect is approximately as great as that produced by equal amounts of codeine.

Dosage

Dextromethorphan hydrobromide is administered orally. The average dose for adults is 10 to 20 mg, one to four times daily. This dose is reduced to one-half for children over 4 years of age and to one-quarter for children under 4 years of age.

Preparations for use as stated for the foregoing drug are marketed under the following name: Romilar Hydrobromide.

Hoffman-La Roche, Inc., cooperated by furnishing scientific data to aid in the evaluation of dextromethorphan hydrobromide.

—*J. Am. Med. Assoc.* *162*:205 (Sept. 15) 1956.

Preparations

Syrup Dextromethorphan (Romilar) Hydrobromide 10 mg. per 4 ml.; 4 ounce, 16 ounce, and 1 gallon bottles.

Tablets Dextromethorphan (Romilar) Hydrobromide 10 mg.

Dimenhydrinate

Dramamine®
Intramuscular Use For
Postoperative Nausea and Vomiting

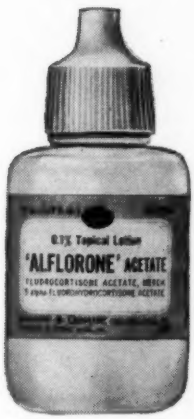
The Council has evaluated the use of dimenhydrinate administered intramuscularly for the prevention and control of postoperative and postanesthetic nausea and vomiting. Because episodes of nausea or emesis after surgery are related to a great many causative and conditioning factors and represent wide ranges in type and severity, the Council found it difficult to arrive at a definite conclusion that would apply to all cases. In a series of over 9,000 unselected cases under partially controlled conditions of routine hospital practice and

'Co-Deltra'
(Prednisone, Buffered)
1956

'Co-Hydeltra'
(Prednisolone, Buffered)
1956

Deltra®
(Prednisone, Merck)
1955

'Hydeltra'
(Prednisolone, Merck)
1955



Alflorone®
Acetate
(Fludrocortisone Acetate, Merck)
1954

for a complete Rx stock

Multiple Compressed Tablets of 'Co-Deltra' and 'Co-Hydeltra' are two new antacid-steroid formulations designed to minimize the gastric distress often encountered with prednisone and prednisolone. CO-DELTRA, CO-HYDELTRA, DELTRA, HYDELTRA, ALFLORONE, HYDROCORTONE and CORTONE represent important prescription volume. Stock the complete line and be assured of unquestioned acceptance by both physician and patient.

HydroCortone®
(Hydrocortisone, Merck)
1952

Cortone®
Acetate
(Cortisone Acetate, Merck)
1950

MSD

MERCK SHARP & DOHME
DIVISION OF MERCK & CO., Inc.
PHILADELPHIA 1, PA.

with all types of anesthetic agents and a variety of operative procedures, dimenhydrinate reduced the incidence of postoperative nausea and vomiting by approximately 50%. Conversely, a negative conclusion regarding its value has been reached in a smaller (85-patient), more accurately controlled series in which nitrous oxide and ether anesthesia were used. It is therefore apparent that the usefulness of dimenhydrinate for this purpose is unsettled. The majority of experts in this field seem to agree, however, that even if a slight reduction in postoperative nausea and vomiting can be proved statistically, the disadvantages of hypotension and longer postoperative sleeping time caused by administration of dimenhydrinate may conceivably outweigh its usefulness for this purpose.

Only the intramuscular route has been employed for the prevention and control of postoperative nausea and vomiting. The usual doses for adults vary. Some clinicians inject 50 mg. before surgery, 50 mg. after surgery, and then 50 mg. every 4 hours for four doses. For children under 5 years of age, all dosages are reduced to 25 mg. Other clinicians have employed a standard dose of 100 mg. for adults, injected shortly before completion of surgery.

The Council voted to amend the monograph on dimenhydrinate in New and Nonofficial Remedies accordingly to describe the intramuscular use of the drug for postoperative nausea and vomiting.

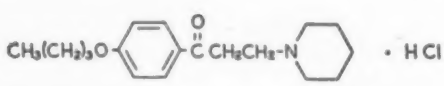
G. D. Searle & Company cooperated by furnishing scientific data to aid in the evaluation of the intramuscular use of dimenhydrinate for postoperative nausea and vomiting.

—*J. Am. Med. Assoc.* 161:1395 (Aug. 4) 1956.

Dyclonine Hydrochloride

Dyclone® Hydrochloride

DYCLONINE HYDROCHLORIDE is 4′-butoxy-3-piperidinopropiophenone hydrochloride.—The structural formula of dyclonine hydrochloride may be represented as follows:



Actions and Uses

Dyclonine hydrochloride, a topical anesthetic agent, differs from most drugs of this pharmacological class in that it does not contain the ester or amide linkage typical of compounds such as procaine. Its systemic toxicity is low; in man and experimental animals, relatively large oral or intravenous doses produce little alteration in respiration, blood pressure, or pulse. No changes referable to inhibition of the parasympathetic nervous system are discernible. The drug also has antimicrobial properties; however, since this action has been established only by in vitro tests, its possible clinical significance is undetermined at present.

Dyclonine hydrochloride is usually an effective anesthetic agent when applied topically to the skin or mucous membranes. The onset of action is rapid, and the intensity and duration of anesthesia compares favorably to that of compounds of the procaine type. The drug is useful in dermatological practice for the treatment of skin conditions in which relief of pain and pruritus is desired. It also may be used for the symptomatic treatment of minor burns and minor trauma, for relief of postoperative discomfort such as occurs after episiotomy, and for symptomatic management of pruritus ani or vulvae. The drug also has been used to anesthetize mucous membranes prior to instrumentation, as for example, before laryngoscopy, bronchoscopy, esophagoscopy, proctoscopy, and systoscopy. When instilled into the conjunctiva, it affords anesthesia without producing miosis or mydriasis.

Although longer clinical experience is necessary to determine its ultimate potentiality as an allergen, at present there are no reports of true sensitization or hypersensitivity to dyclonine hydrochloride. Likewise, the drug has not produced cross sensitization with other local anesthetic agents, a characteristic that may be the result of the differences in chemical structure. To date, irritation at the site of local application has been the only significant side-effect to its administration. Despite its low systemic toxicity, sufficient evidence is at hand to justify its use only by topical application.

Dosage

Dyclonine hydrochloride is administered topically in a 1% concentration in a vanishing cream base or as a 0.5% aqueous solution. It is applied as necessary to the skin or mucous membranes in amounts necessary to cover the painful or pruritic surfaces.

Preparations for use as stated for the foregoing drug are marketed under the following name: Dyclone.

Pitman-Moore Company, Division of Allied Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of dyclonine hydrochloride.

—*J. Am. Med. Assoc.* 162:116 (Sept. 8) 1956.

Preparations

Cream Dyclonine (Dyclone) Hydrochloride 1 percent; 30 Gm. tubes.

Solution Dyclonine (Dyclone) Hydrochloride 0.5 percent; 30 ml. and 240 ml. bottles.

Gitalin (Amorphous)

Gitaligin®
Intravenous Use

The Council has evaluated the usefulness of gitalin (amorphous) by the intravenous route. On the basis of currently available evidence, the Council concluded that the intravenous injection of this glycoside preparation is useful for the rapid digitalization of adult patients in whom the oral route is not feasible, especially those with acute, congestive cardiac decompensation. The average initial dose by the route is 2.5 mg. twice in 24 hours. The usual total digitalizing dose is about 5 to 6 mg. After full digitalization, when maintenance by the parenteral route is indicated, intravenous administration of doses as high as 2.5 mg. twice weekly have been used, although intravenous injection of 0.5 mg. daily may be adequate. However, oral maintenance therapy of 0.5 mg. daily should be substituted as soon as possible. Intravenous administration should be done with caution and in reduced dosage if the patient has received other digitalis drugs within the previous 2 weeks.

The Council voted to amend New and Nonofficial remedies accordingly to describe this additional route of administration.

White Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of the intravenous use of gitalin (amorphous).

—*J. Am. Med. Assoc.* 162:117 (Sept. 8) 1956.

Hospital personnel, as well as the patient, benefit during the use of effective, economical, timesaving, patient-saving diuretics—MERCUHYDRIN and NEOHYDRIN. NURSES—because patients are out of bed earlier, require less care. PHYSICIANS—because this diuretic combination is dependable insurance against relapses. And YOU—THE HOSPITAL ADMINISTRATOR—because MERCUHYDRIN and NEOHYDRIN shorten hospital stays, ease bed shortages.

a standard for initial control of severe failure

MERCUHYDRIN® SODIUM
BRAND OF MERALLURIDE INJECTION

for nonrelapsing oral diuretic maintenance

NEOHYDRIN® TABLET BRAND OF CHLORMERODRIN

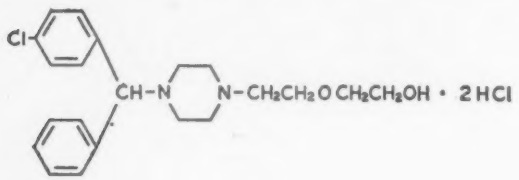
LAKESIDE

01888

Hydroxyzine Hydrochloride

Atarax® Hydrochloride

HYDROXYZINE HYDROCHLORIDE is 1-(*p*-chlorobenzhydryl)-4-[2-(2-hydroxyethoxy)ethyl]piperazine dihydrochloride.—The structural formula of hydroxyzine hydrochloride may be represented as follows:



Actions and Uses

Hydroxyzine hydrochloride, which is similar in chemical structure and pharmacological action to some of the antihistamines, produces depression of the central nervous system. Sedation is the most prominent action of hydroxyzine hydrochloride and forms the basis for its clinical use. The drug also appears to exert some actions similar to those of chlorpromazine; however, these are not sharply enough defined to permit pharmacological classification as a chlorpromazine-like drug.

Hydroxyzine hydrochloride has been employed clinically as a tranquilizing or calming agent for the symptomatic treatment of a wide variety of emotional or mental disorders characterized by anxiety, tension, and agitation; however, sufficient experience has not been gained to determine its ultimate usefulness as a psychotherapeutic agent. To date, its use in patients with frank psychoses has not been promising. The drug is likewise of little benefit in depressive states unless there is a strong overlay of agitation and anxiety. On the basis of currently available evidence, it would appear to be useful for the symptomatic management of neuroses rather than psychoses.

The toxicity of hydroxyzine hydrochloride is low. Drowsiness may occur shortly after the drug is taken but is transient and apparently never proceeds into true sleep. This effect, as distinguished from the tranquilizing action of the drug, seems to diminish in frequency and intensity upon prolonged administration.

Dosage

Hydroxyzine hydrochloride is administered orally. The usual dose for adults is 25 mg. three times daily, but this may vary in amount and frequency according to severity of symptoms and individual response. For children between 6 and 12 years of age, doses of 10 mg. twice a day have been employed. This may be increased to 10 mg. three to four times daily if necessary. Sufficient experience is not available to state dosage requirements for infants or children under the age of 6.

Preparations for use as stated for the foregoing drug are marketed under the following name: Atarax Hydrochloride.

J. B. Roerig and Company, Division of Chas. Pfizer & Company, Inc., cooperated by furnishing scientific data to aid in evaluation of hydroxyzine hydrochloride.

—*J. Am. Med. Assoc.* *162*:205 (Sept. 15) 1956.

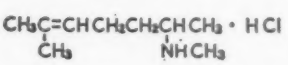
Preparations

Tablets Hydroxyzine (Atarax) Hydrochloride 10 mg. and 25 mg., sugar coated.

Isometheptene Hydrochloride

Octin® Hydrochloride

ISOMETHEPTENE HYDROCHLORIDE is 2-methylamino-6-methyl-5-heptene hydrochloride.—The structural formula of isometheptene hydrochloride may be represented as follows:



Actions and Uses

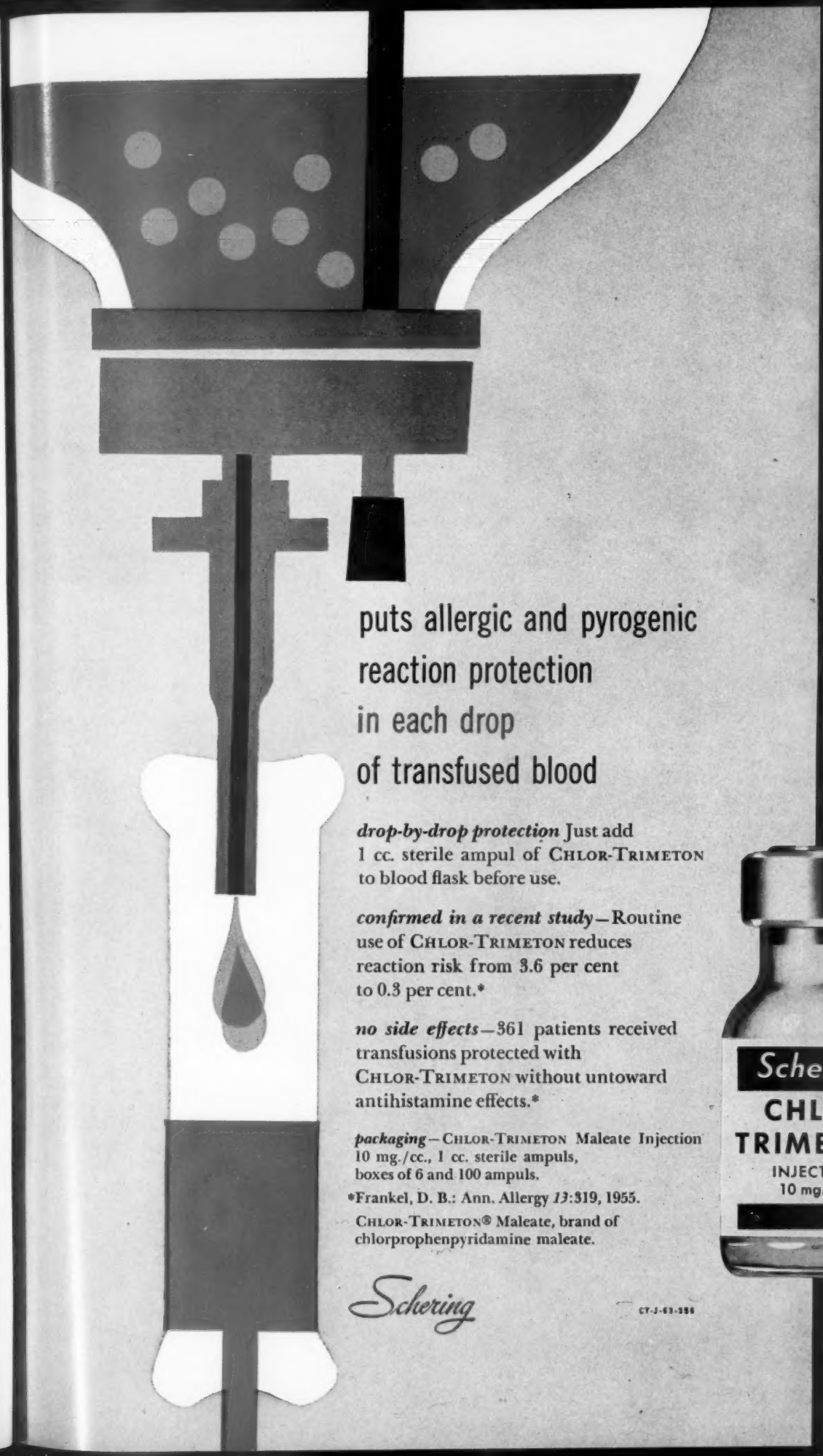
Isometheptene hydrochloride, an unsaturated aliphatic amine, exhibits antispasmodic and vasoconstrictor properties. Thus, in experimental animals it produces relaxation of smooth muscle of hollow organs, including the urinary and gastrointestinal tract and the sphincters of the bile duct, pancreatic duct, and urinary bladder. Its antispasmodic effect on these structures is caused by stimulation of sympathetic (inhibitory) nerve endings rather than by inhibition of parasympathetic endings, as with atropine. The drug resembles epinephrine in that it produces moderate peripheral vasoconstriction, an increase in the contractile force of the myocardium, and a transient increase in blood pressure. Other effects include a slight bronchodilation, mydriasis, respiratory stimulation, and a shrinkage of nasal and pharyngeal mucosa. Isometheptene hydrochloride therefore may be classified as a sympathomimetic amine.

On the basis of these pharmacological studies, isometheptene hydrochloride has been employed clinically for the treatment of urinary tract spasm and spastic conditions of the gastrointestinal tract and its sphincters, as well as for the relief of migraine-like headache and other conditions believed to be caused by vasodilation in the cranial and cerebral vascular beds. Although it is the clinical impression of some physicians that patients with such conditions are benefited, convincing evidence is lacking to indicate that the drug, rather than the natural course of the disease is responsible for alleviation of symptoms. Thus, the usefulness of isometheptene hydrochloride for relieving the pain of ureteral colic, as an aid in the passage of stone, for facilitating instrumentation during urologic or gastrointestinal examination, for relaxing gastrointestinal spasm, or for the alleviation of migraine or tension headache or histaminic cephalalgia is unsettled. Since pharmacological studies indicate that it may have some use in such conditions, and since it is of low clinical toxicity, its therapeutic trial may be justified in appropriate cases.

After parenteral administration of isometheptene hydrochloride, the most common side-effect is a rise in blood pressure, particularly in patients with a labile vascular system. This occurs much less frequently after oral administration. Other minor side-effects, which are rare and transient, include lightheadedness, nervousness, and sometimes nausea. The drug is contraindicated in all hypertensive patients. Initial parenteral administration should follow injection of a small test dose with subsequent careful checks on blood pressure.

Dosage

Isometheptene hydrochloride is administered orally or intramuscularly. The usual oral dose for adults is 15 to 20 drops of a 10% solution (containing 100 mg. per cubic centimeter) every half hour for a total of four doses. By the intramuscular route, 50 to 100 mg.



puts allergic and pyrogenic reaction protection in each drop of transfused blood

drop-by-drop protection Just add 1 cc. sterile ampul of CHLOR-TRIMETON to blood flask before use.

confirmed in a recent study—Routine use of CHLOR-TRIMETON reduces reaction risk from 3.6 per cent to 0.3 per cent.*

no side effects—361 patients received transfusions protected with CHLOR-TRIMETON without untoward antihistamine effects.*

packaging—CHLOR-TRIMETON Maleate Injection 10 mg./cc., 1 cc. sterile ampuls, boxes of 6 and 100 ampuls.

*Frankel, D. B.: Ann. Allergy *13*:319, 1955.

CHLOR-TRIMETON® Maleate, brand of chlorprophenpyridamine maleate.

Schering

CT-J-63-355

is injected for the control of acute pain in adults, but oral therapy should be substituted as soon as possible. The drug should never be injected intravenously.

Preparations for use as stated for the foregoing drug are marketed under the following name: Octin Hydrochloride.

Bilhuber-Knoll Corp. cooperated by furnishing scientific data to aid in the evaluation of isometheptene hydrochloride.

—*J. Am. Med. Assoc.* 162:206 (Sept. 15) 1956.

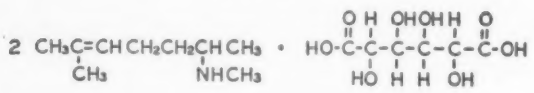
Preparations

Injection Isometheptene (Octin) Hydrochloride 100 mg. per ml.; 1 ml. ampuls.

Solution, Oral, Isometheptene (Octin) Hydrochloride 100 mg. per ml.; 30 ml. bottles.

Isometheptene Mucate — Octin® Mucate

ISOMETHEPTENE MUCATE is 2-methylamino-6-methyl-5-heptene mucate.—The structural formula of isometheptene mucate may be represented as follows:



Actions and Uses

Isometheptene mucate has the same actions and uses as the hydrochloride salt. (See the monograph on isometheptene hydrochloride.) Because it is not used by the parenteral route, it rarely causes hypertension.

Dosage

Isometheptene mucate is administered orally or rectally. The usual oral dose for adults is 0.12 gm. every half hour for a total of four doses. Alternatively, one suppository containing 0.25 gm. may be inserted into the rectum; this procedure may be repeated in one hour if necessary.

Preparations for use as stated for the foregoing drug are marketed under the following name: Octin Mucate.

Bilhuber-Knoll Corp. cooperated by furnishing scientific data to aid in the evaluation of isometheptene mucate.

—*J. Am. Med. Asso.* 162:206 (Sept. 15) 1956.

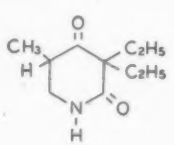
Preparations

Suppositories, Rectal, Isometheptene (Octin) Mucate 0.25 Gm.

Tablets Isometheptene (Octin) Mucate 0.13 Gm.

Methyprylon — Noludar®

METHYPRYLON is 3,3-diethyl-5-methyl-2,4-piperidinedione. The structural formula of methyprylon may be represented as follows:



Actions and Uses

Methyprylon, a piperidine derivative, is chemically unrelated to the barbiturates but depresses the central nervous system in a similar manner. The drug possesses a wide margin of safety and exerts pronounced hypnotic effects but has less tendency to produce respiratory depression than barbiturates. The onset and duration of its action are comparable to those of such short-acting barbiturates as secobarbital sodium and pentobarbital sodium. The possibility of addicting properties after long-term administration has not been fully assessed, but present clinical information indicates this to be less likely than with the barbituric acid derivatives.

Methyprylon is useful as a hypnotic in patients with simple and nervous insomnia. Although it is not superior to the barbiturates in this respect, it is well accepted by patients and appears to approximate the hypnotic potency of the usual doses of secobarbital sodium or pentobarbital sodium. Thus, its soporific action begins shortly after administration and generally lasts several hours. In most patients, this is sufficient to induce a restful night's sleep.

The ultimate usefulness of methyprylon as a tranquilizing agent or as a daytime sedative is unsettled at the present time; however, available clinical evidence indicates that it is promising in this respect since it is the impression of both physicians and patients that the drug does exert a sedative action, especially in cases of anxiety and tension. Its action in patients with cardiac neuroses, nervous manifestations of the menopause, or hypertension is not established, and no information is available concerning its use as a preoperative sedative.

Side-effects so far reported from therapeutic doses of methyprylon have been infrequent and mild. These include occasional instances of vertigo and nausea and vomiting, none of which appears to be of great significance. In addition, hangover is less prominent than after the barbiturates. In the body, methyprylon is dehydrogenated to a tetrahydropyridine compound that appears in the urine in greater concentration than the parent drug. This analogue also appears in the bile. Since an analogous tetrahydropyridine has been implicated as a causative agent in agranulocytosis, caution should be exercised in administering methyprylon. To date, however, the drug has been administered to a large number of patients for prolonged periods without evidence of toxic effect on the kidney, liver, bone marrow, or the hematopoietic system.

Dosage

Methyprylon is administered orally. The usual hypnotic dose for adults is 0.2 to 0.4 gm. at bedtime. Doses of 50 to 100 mg. three or four times daily have been employed for daytime sedation. Dosage for children is reduced proportionally.

Preparations for use as stated for the foregoing drug are marketed under the following name: Noludar.

Hoffmann-La Roche, Inc., cooperated by furnishing scientific data to aid in the evaluation of methyprylon.

—*J. Am. Med. Assoc.* 161:1384 (Aug. 4,) 1956.

Preparations

Elixir Methyprylon (Noludar) 50 mg. per 4 ml.; 16 oz. and gallon bottles.

Tablets Methyprylon (Noludar) 50 mg. and 200 mg.

in acute and chronic pyelonephritis, cystitis and prostatitis

freedom

from pain, infection and resistant mutants

"Frequently, patients reported symptomatic improvement within 24 hours."[1] Furadantin "may be unique as a wide-spectrum antimicrobial that . . . does not invoke resistant mutants."[2]

Comparative Sensitivity to Furadantin of Infectious Microorganisms Isolated over a Two-Year Period[3]

Microorganism	Total no. strains	Sensitive*		Moderately sensitive*		Resistant*	
		No.	Per cent of total	No.	Per cent of total	No.	Per cent of total
Proteus vulgaris	237	209	88.2	28	11.8	0	0
Escherichia coli (including paracolon bacillus)	281	255	92.7	23	8.2	3	1.1
Aerobacter aerogenes	223	183	82.1	40	17.9	0	0
Streptococcus faecalis	160	155	96.7	5	3.1	0	0
Pseudomonas aeruginosa	101	5	5.0	40	39.9	56	55.4
Micrococcus pyogenes var. aureus	6	6	100	0	0	0	0
Klebsiella pneumoniae	3	3	100	0	0	0	0
Alcaligenes faecalis	2	2	100	0	0	0	0

*Organisms inhibited by 100 μg./ml. or less are classified as sensitive, by 200 to 400 μg./ml. as moderately sensitive, and those not inhibited by 400 μg./ml. as resistant.

"The status of P. vulgaris and of M. pyogenes var. aureus is especially noteworthy in the light of the high degree of resistance exhibited by those organisms to antibiotics currently employed."[3]

REFERENCES: 1. Trafton, H. M., et al.: N. England J. M. **252**:383, 1955. 2. Waisbren, B. A., and Crowley, W.: A. M. A. Arch. Int. M. **95**:653, 1955. 3. Schneierson, S. S.: Antibiotics **3**:212, 1956.

Furadantin®

BRAND OF NITROFURANTOIN

FURADANTIN DOSAGE:
Average adult dose is 100 mg., q.i.d. (at mealtime, and on retiring, with food or milk). Average daily dosage for children is 5 to 7 mg./Kg. in four divided doses.

EATON LABORATORIES
Norwich New York

SUPPLIED:
Tablets, 50 and 100 mg., bottles of 25 and 100.
Oral Suspension, 5 mg., per cc., bottle of 118 cc.

NITROFURANS—a new class of antimicrobials—neither antibiotics nor sulfonamides

Poliomyelitis Immune Globulin (Human)

Use of in Treatment of Agammaglobulinemia or Hypogammaglobulinemia

The Council was requested to evaluate the usefulness of poliomyelitis immune globulin (human) for the treatment of agammaglobulinemia or hypogammaglobulinemia. This syndrome, which may occur in both adults and children, is characterized by an acquired or congenital absence of deficiency of gamma globulin, the serum fraction that contains most of the antibodies. A diagnosis of agammaglobulinemia or hypogammaglobulinemia may be entertained on the basis of repeated bacterial infections, the absence of isohemagglutinins, and a comparative inability of antibiotics to combat these infections. Confirmation may be obtained by determination of the serum gamma globulin level. In such cases it appears logical, therefore, to attempt to control clinical symptoms by the administration of compatible, but exogenous, immune gamma globulin. On the basis of currently available evidence, the Council concluded that routine "replacement" therapy with poliomyelitis immune globulin (human) is useful for the treatment of this syndrome. The immunity thus provided is temporary and passive; continued protection depends on routine and regular administration of the immune globulin. Although data were considered on poliomyelitis immune globulin (human) only, the Council was aware that the older preparation, immune serum globulin, is equally effective for the treatment of patients with this condition. The Council further concluded that, insofar as the other serum antibodies are concerned, poliomyelitis immune globulin (human) is equivalent to immune serum globulin and that both preparations can be used interchangeably in patients with agammaglobulinemia or hypogammaglobulinemia. For this purpose the preparations are administered by deep intramuscular injection, preferably in the gluteus. No arbitrary dosage schedule has as yet been determined. Judicious management of dosage should be on an individual basis with an attempt to determine for each patient the lowest dose required for his protection. Likewise, the interval between injections must be individually determined. Factors such as the age and weight of the patient, his general state of health, and the bacterial and viral antigens to which he has been exposed should be taken into consideration. As a general pattern, monthly injections of 30 to 50 cc. for adults and 20 to 40 cc. for children may be given; however, it is possible that doses much smaller than these may be adequate with less discomfort to the patient.

The Council voted to amend New and Nonofficial Remedies accordingly to describe the use of poliomyelitis immune globulin (human) and immune serum globulin for the treatment of agammaglobulinemia and hypogammaglobulinemia.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of the usefulness of poliomyelitis immune globulin (human) for the treatment of agammaglobulinemia or hypogammaglobulinemia.

—*J. Am. Med. Assoc.* 162:117 (Sept. 8) 1956.

Poliomyelitis Vaccine

POLIOMYELITIS VACCINE is a formaldehyde-inactivated vaccine containing approximately equal parts of aqueous suspensions of individually tissue-cultured type 1, type 2, and type 3 strains of poliomyelitis virus approved by the National Institutes of Health. The vaccine is tested for antigenic potency and for nonviability of component viruses in accordance with requirements promulgated by the National Institutes of Health.

Actions and Uses

Poliomyelitis vaccine is used to induce artificial active immunity against paralytic poliomyelitis on the basis of its ability to stimulate the production of protective levels of antibodies in susceptible animals and in man. Observations on the protective effect of the vaccine as currently prepared are thus far inadequate to make it possible to reach final conclusions regarding the extent or duration of immunity that can be expected from its use. Its protective effect against nonparalytic forms of poliomyelitis infection and its influence upon the subsequent acquisition of natural immunity to the disease also have not been elucidated. Prior clinical trial with a similar preparation in school children of the most susceptible age group and epidemiological observations on the effect of the 1955 preparations suggest that the vaccine is capable of reducing the incidence of paralytic poliomyelitis by approximately 60 to 80%.

Poliomyelitis vaccine is as safe and as effective as can reasonably be expected. If possible, it is advisable to complete inoculations prior to the expected seasonal increase in the incidence of the disease. The presence of acute poliomyelitis in a community is not considered a contraindication to use of the vaccine in presumably unexposed but susceptible individuals; however, on the basis of present knowledge, it seems inadvisable to inoculate family contacts. Experience so far has not indicated that there is a provocative effect from inoculation with the vaccine.

Poliomyelitis vaccine should be employed with the usual precautions for vaccines in general. Local and systemic reactions after inoculation of the vaccine generally are mild and infrequent. General malaise and low-grade fever of short duration may be observed occasionally. The presence of small amounts of penicillin and streptomycin in the vaccine has not been associated with severe allergic reactions, except possibly in rare instances. So far, allergic reactions have been of a minor nature, and even inoculated subjects with known sensitivity to these antibiotics usually have not reacted adversely. In highly allergic persons, a test dose of the vaccine may be injected intradermally so that the effect can be observed before administration of the usual dose is attempted. The elimination of penicillin and streptomycin or its derivatives from the current preparation is advised by some authorities to eliminate the possibility that its use may sensitize some individuals; others feel that the amounts present in the vaccine are too small to be of significance and are no greater than the amounts found in milk from cows fed with antibiotics. The theoretical possibilities that the vaccine might be capable of inducing the formation of harmful Rh, kidney tissue, and animal serum antibodies so far have not been realized. The vaccine also has not been associated with other toxic reactions or neurological

ACTH
q 2 days
rather than q 12 h

One injection is effective for 24 to 72 hours or more

By adsorption of ACTH on zinc hydroxide, Cortrophin-Zinc permits extension of ACTH activity for a period of 1 to 3 days. This minimizes the therapeutic "ups and downs" which may occur during ACTH-in-gel therapy and provides smooth corticotropin action for a truly extended period.

Cortrophin-Zinc is easier to handle than gelatin preparations. An aqueous suspension, it flows easily through a 26-gauge needle, eliminating preheating, clogging syringes, and heavy-gauge needles that add to the pain.

Cortrophin-Zinc is supplied in 5 cc vials each cc containing 40 U.S.P. units of corticotropin with 2 mg. of zinc.

CORTROPHIN* ZINC†

a development of **Organon Inc.**
ORANGE, N. J.

*T.M.—Cortrophin Available in other countries as Cortrophine-Z †Patent Pending

sequelae such as polyneuritis, radiculitis, and encephalopathy. While these are theoretically possible, poliomyelitis vaccine contains less protein than other vaccines in use and is not considered to involve any greater potential risk from this standpoint.

It should be apparent from the relatively short period of time over which the vaccine has been developed and used, as compared to established immunologic agents effective in the prevention of other infections, that its ultimate usefulness can be determined only after longer experience has been gained. Physicians and health officers should be alert to the need for confirmatory laboratory findings in the diagnosis of doubtful cases of poliomyelitis to insure accurate reporting of cases and correct interpretation of the effect of the vaccine. Careful observations of all previously inoculated subjects will speed the accumulation of knowledge essential for the further evaluation of the vaccine. These might well include records of lot numbers of the vaccine used, sites of injection employed, the exact course of weakness or paralysis, and other details of confirmatory findings should poliomyelitis occur in inoculated subjects.

Dosage

Poliomyelitis vaccine is injected subcutaneously or intramuscularly. Intradermal injection has not been sufficiently studied to justify that method of inoculation. Primary vaccination as currently suggested consists of two 1-cc. doses spaced at an interval of two or preferably four to six weeks and a third dose of 1 cc. not less than seven months after the second. Until more is known about the duration of the effect of the vaccine, the need for follow-up inoculations cannot be definitely determined.

The vaccine should be stored at a temperature between 2 and 10 C, preferably at 2 C, but should not be allowed to freeze. Changes in color of the vaccine under these conditions do not appear to alter its initial potency and safety. It should not be used if there is any evidence of turbidity.

Preparations for use as stated for the foregoing drug are marketed under the following name: Poliomyelitis Vaccine.

Eli Lilly and Company; Pitman-Moore Company, Division of Allied Laboratories, Inc.; Merck Sharp & Dohme, Division of Merck & Co., Inc.; Wyeth Laboratories, Division of American Home Products Corporation; Public Health Service, U. S. Department of Health, Education and Welfare; Dr. Jonas E. Salk; and Dr. Herbert Ratner cooperated by furnishing scientific data to aid in the evaluation of poliomyelitis vaccine.

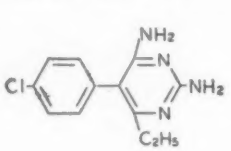
—*J. Am. Med. Assoc.* **162**:115 (Sept. 8) 1956.

Preparations

Injection Poliomyelitis Vaccine 1 ml., 3 ml., and 9 ml.

Pyrimethamine — Daraprim®

PYRIMETHAMINE is 2,4-diamino-5-*p*-chlorophenyl-6-ethylpyrimidine.—The structural formula of pyrimethamine may be represented as follows:



Actions and Uses

Pyrimethamine, a diaminopyrimidine chemically related to chloroguanide hydrochloride, is a potent folic acid antagonist used as an antimalarial agent. Its antimalarial action is believed to be due to a differential requirement between host and parasite for the nucleic acid precursors involved in growth. The drug is effective as a suppressive agent in malignant tertian (Plasmodium falciparum) malaria and benign tertian (P. vivax) malaria. Against overt infections, it is a slowly acting schizonticide. It interrupts transmission of the disease by arresting sporogony in the mosquito. Pyrimethamine is primarily useful, therefore, for the prevention of clinical attacks of both vivax and falciparum malaria and in preventing transmission by arresting sporogony. There also is evidence to indicate that, when a suppressive regimen is continued for a sufficient number of weeks to extend through the time when relapses would be expected, eradication ("suppressive cure") of vivax infections may result. The use of pyrimethamine as a suppressive agent in falciparum infections results in radical cure in most cases. Because of its onset of action, pyrimethamine should not be used for the treatment of acute primary attacks. For such attacks, a fast-acting schizonticide is indicated.

Primary resistance to the drug does not develop during its clinical use as a suppressant in the recommended dosage; however, cross resistance to pyrimethamine may develop in plasmodial strains that are already resistant to chloroguanide. The latter condition is usually the result of improper usage. Plasmodial strains that are resistant to chloroguanide and cross resistant to pyrimethamine have appeared in Malaya and certain other areas of the world where malaria is endemic. For this reason, the drug should be used with caution in areas where chloroguanide has been extensively or improperly used, and it should not be employed at all if the infection is known to be due to strains resistant to chloroguanide.

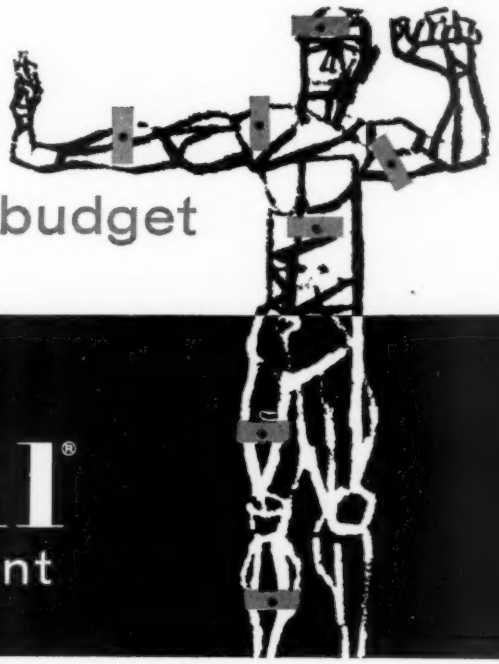
Pyrimethamine has a wide margin of safety, and, in therapeutic doses, its toxicity is very low; however, since the drug is a folic acid antagonist, gross and prolonged overdosage may produce toxic effects associated with folic acid deficiency. These include a megaloblastic anemia and, less commonly, leukopenia, both of which disappear rapidly when administration of the drug is discontinued.

Dosage

Pyrimethamine is administered orally. In contrast to quinine or other antimalarials, it is tasteless. The usual dose for adults for suppressive prophylaxis is 25 mg. each week. This dosage should be continued indefinitely in areas where malaria is prevalent. The dosage for children under 15 years of age is 12.5 mg. weekly. If the regimen for suppressive prophylaxis is extended throughout all periods of exposure to malaria and through the expected periods of early recrudescence, suppressive cure of vivax infections may be obtained. The minimum time to achieve this result is usually 10 weeks. If late-relapsing strains are involved, a much longer period may be required for suppressive cure. If the characteristic time of relapse is known for a late-relapsing strain, the initial course of suppressive prophylaxis may be followed by another course of pyrimethamine during the period in which relapse is characteristically expected. Although pyrimethamine is not intended for therapy of acute attacks, it may be administered concomitantly

NEW! improved
TOPICAL ENZYME THERAPY

with practical
advantages
for the hospital budget



Panafil®
ointment

for wounds, ulcers, burns

PANAFIL Ointment is an efficient enzymatic debriding agent with the added property of promoting healthy granulation. Safe for out-patient use as well as for bed patients, PANAFIL now makes topical enzyme therapy an economical routine procedure.

fewer dressings and less supervision required

PANAFIL's ready-to-use ointment form saves the pharmacist valuable preparation time. Because continuous dressings are employed, it reduces nursing care. A recent study* on the treatment of decubitus ulcers among paraplegics shows that PANAFIL dressings b.i.d. save 18⅔ hours nursing time per patient per week over saline soaks and bland ointment q.i.d.

PANAFIL is economical—Price to hospitals on direct purchase:

PANAFIL Ointment, 1 oz. tube	$1.20
4 oz. tube	3.20
1 lb. jar	8.00

(1 oz. and 4 oz. slightly higher if purchased through wholesaler)

Composition: PANAFIL Ointment contains papain powder 10%, urea U.S.P. 10%, and water-soluble chlorophyll derivatives N.N.R. 0.5% in a hydrophilic base.

*Data to be published by government hospital.

Samples and literature available upon request.

Rystan company · Mount Vernon, New York 27256

with a fast-acting schizonticide to initiate transmission control by arresting sporogony in the mosquito. The dosage for this purpose is 25 mg. daily for the first two days. After remission of the acute attack, the usual suppressive prophylactic dose of 25 mg. (12.5 mg. for children) each week should be resumed.

Preparations for use as stated for the foregoing drug are marketed under the following name: Daraprim.

Burroughs Wellcome & Company, Inc. cooperated by furnishing scientific data to aid in the evaluation of pyrimethamine.

—*J. Am. Med. Assoc.* *161*:1384 (Aug. 4) 1956.

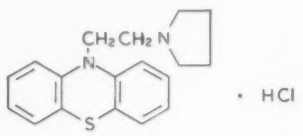
Preparations

Tablets Pyrimethamine (Daraprim) 25 mg., scored, foil-wrapped.

Pyrathiazine Hydrochloride

Pyrrolazote® Hydrochloride

PYRATHIAZINE HYDROCHLORIDE is 10-[2-(1-pyrrolidyl)-ethyl]phenothiazine hydrochloride.—The structural formula of pyrathiazine hydrochloride may be represented as follows:



Actions and Uses

Pyrathiazine hydrochloride, a phenothiazine compound chemically related to promethazine hydrochloride, is an effective antihistaminic agent with actions, uses, and side-effects similar to those of other drugs of this pharmacological class. A slight degree of nausea also may follow its admistration. The development of agranulocytosis has been reported after administration of doses greatly in excess of therapeutic levels for periods of longer than a month. Blood cell counts should therefore be made at intervals in patients receiving this drug for long periods. (See the general statement on histamine-antagonizing agents in New and Nonofficial Remedies.)

Dosage

Pyrathiazine hydrochloride is administered orally. The usual dose for adults is 25 to 50 mg. three or four times daily, preferably after meals and at bedtime. For children over 4 years of age, a dose of 12.5 to 25 mg. three or four times daily as required may be employed.

Preparations for use as stated for the foregoing drug are marketed under the following name: Pyrrolazote.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of pyrathiazine hydrochloride.

—*J. Am. Med. Assoc.* *161*:1384 (Aug. 4) 1956.

Preparations

Capsules Pyrroxate containing Pyrathiazine (Pyrrolazote) Hydrochloride 12.5 mg., Methoxyphenamine (Orthoxine) Hydrochloride 25 mg., Acetophenetidin 150 mg., Acetylsalicylic Acid 210 mg., and Caffeine 30 mg. Pyrroxate Capsules are also available containing Codeine Phosphate 15 mg. (¼ gr.).

Tablets Pyrathiazine (Pyrrolazote) Hydrochloride 25 mg. and 50 mg., sugar coated.

Tablets Pyrathiazine (Pyrrolazote) Hydrochloride, Laminated (prolonged action) 50 mg.

Sodium Acetrizoate

Urokon® Sodium

Use for Cerebral Angiography

The Council was requested to evaluate the usefulness and safety of sodium acetrizoate for cerebral angiography. This water-soluble organic iodine compound previously has been found suitable as a contrast medium for intravenous (excretory) urography, retrograde (transureteral) pyelography, intravenous nephrography and angiocardiography, translumbar arteriography, and intraductal cholangiography. On the basis of currently available evidence, the Council concluded that it is also useful for the visualization of the cerebral arteries; however, sufficient evidence and clinical experience have not been accumulated to permit a definite conclusion regarding its efficacy or toxicity as compared to other agents used for this purpose.

The dosage of sodium acetrizoate for cerebral angiography varies, but in general the total volume administered as a single injection probably should not exceed 10 cc. This is injected as a 30% solution into the external carotid artery immediately before roentgenographic exposure. Severe and dangerous reactions may occur if the 70% solution is injected accidentally; hence, extreme caution should be exercised regarding the proper concentration.

The Council voted to amend New and Nonofficial Remedies accordingly to describe the use of sodium acetrizoate for cerebral angiography.

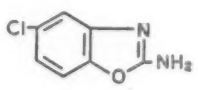
Mallinckrodt Chemical Works cooperated by furnishing scientific data to aid in the evaluation of the use of sodium acetrizoate for cerebral angiography.

—*J. Am. Med. Assoc.* *162*:37 (Sept. 1) 1956.

Zoxazolamine

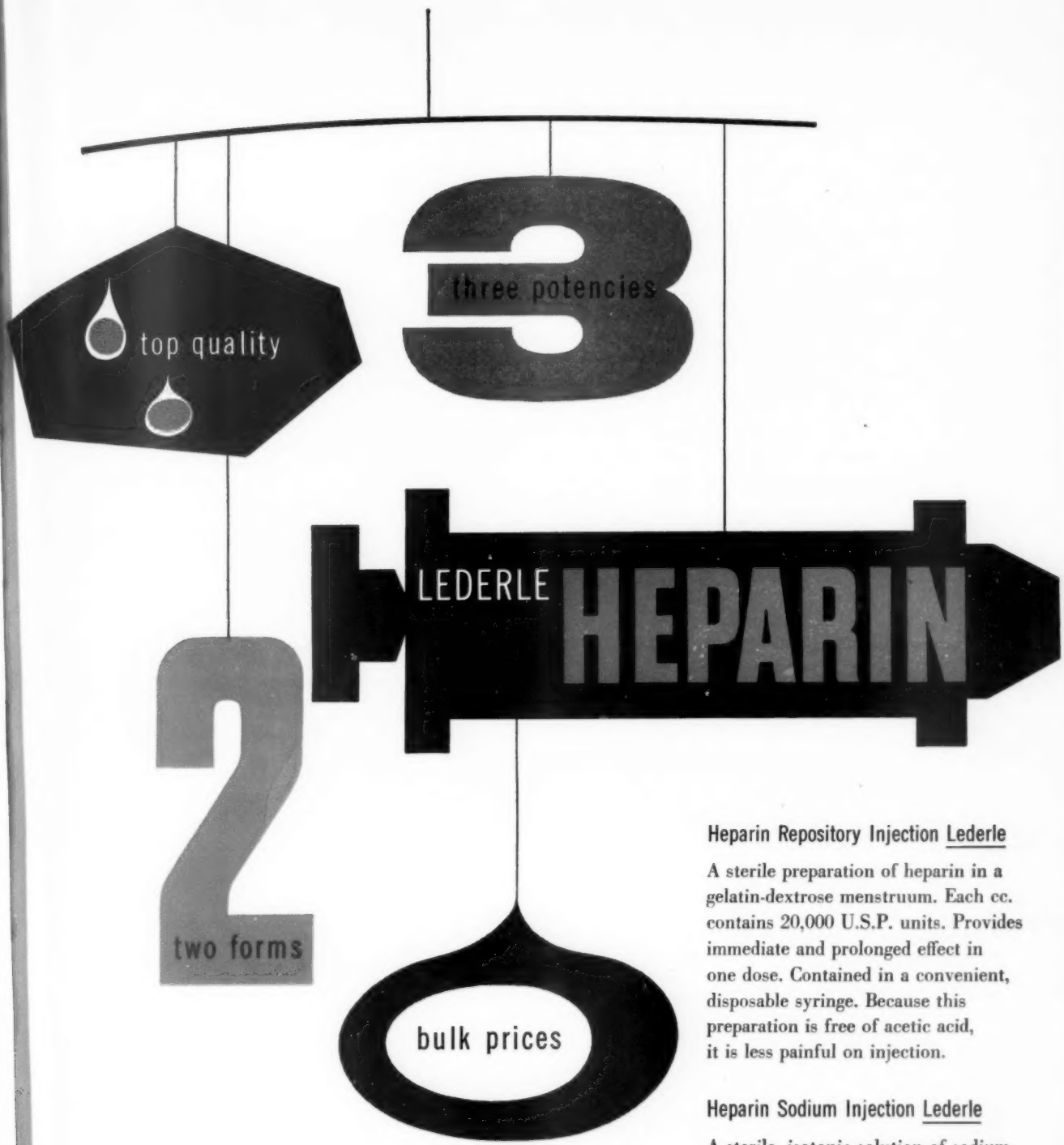
Flexin®

ZOXAZOLAMINE is 2-amino-5-chlorobenzoxazole.—The structural formula of zoxazolamine may be represented as follows:



Actions and Uses

Zoxazolamine, a skeletal muscle relaxant, depresses or interrupts transmission of nerve impulses through polysynaptic pathways. Like mephenesin, its major sites of action are the brain stem, subcortical areas, and the spinal cord. Experiments with animals indicate that the drug has no direct effect on skeletal muscle, nor does it act at the myoneural junction. With experimental methods currently employed, comparatively little effect can be detected on monosynaptic arcs. Zoxazolamine



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LEDERLE LABORATORIES DIVISION
AMERICAN Cyanamid COMPANY
PEARL RIVER, NEW YORK

Heparin Repository Injection Lederle

A sterile preparation of heparin in a gelatin-dextrose menstruum. Each cc. contains 20,000 U.S.P. units. Provides immediate and prolonged effect in one dose. Contained in a convenient, disposable syringe. Because this preparation is free of acetic acid, it is less painful on injection.

Heparin Sodium Injection Lederle

A sterile, isotonic solution of sodium heparin. Available in two potencies: 1,000 U.S.P. units (approximately 10 mg. heparin) per cc. for intravenous therapy with 5% glucose, Ringer's solution, or saline; and 10,000 U.S.P. units (approximately 100 mg. heparin) per cc. for intramuscular therapy.

has a longer duration of action than mephenesin and, in comparable dosage, its spasticity-reducing potency is greater. It likewise is more effective by mouth than mephenesin in equal amounts.

Zoxazolamine has been employed in a wide variety of conditions that may be unrelated in pathogenesis but in which either skeletal muscle spasm or spasticity is present as a common denominator. Of these disease entities, those resulting from musculoskeletal disorders, such as sprains, muscle strains and contusions, low back disorders, fibrositis, bursitis, myositis, and spondylitis, appear to respond best to the drug. A high percentage of patients with these conditions may be expected to be benefited by the drug with attending relief of muscle spasm discomfort. In such conditions, the drug should not be expected to bring about permanent improvement without appropriate attention to the application of suitable physical therapeutic measures. In patients with rheumatoid arthritis and osteoarthritis, the drug is of limited usefulness as an adjunct to salicylate and other forms of therapy. Although the drug may aid in the relief of muscle spasm, the concomitant production of muscular weakness in some cases can result in decreased over-all functional activity. The agent is of questionable usefulness in cervical syndrome.

In general, patients with muscle spasm and spasticity resulting from musculoskeletal disorders appear to respond better to zoxazolamine than those with neurological disease. Of the latter category, beneficial results have been attained chiefly in patients with cerebral involvement, as for example, cerebral palsy and spastic paraplegia. Excluding those cerebral spastic states with athetoid derangements, the drug has been moderately successful in relieving hypertonus of the involved muscle groups in some patients. The more severe type of neurological spasticity states, namely those involving the spinal cord, have so far responded less well to zoxazolamine. These include such conditions as cord injury or neoplastic involvement and multiple sclerosis; results are likewise often disappointing in Parkinson's disease and various pyramidal tract lesions. The drug has no effect on basal ganglion disorders or convulsive diseases such as epilepsy.

Zoxazolamine has a margin of safety greater than that of mephenesin. Excess muscle fatigue, which can occur after administration of both agents, is less pronounced after zoxazolamine. Side-effects to its administration, though frequent and often unpleasant, are not serious and are reversible upon withdrawal of the drug. The most frequent of these are nausea and vomiting; other less frequent side-effects include anorexia, headache, lightheadedness, transient skin rash, malaise, weakness, and drowsiness.

Dosage

Zoxazolamine is administered orally. The usual dosage for adults is 0.25 to 0.5 gm. three or four times daily during meals or with food. For children, a dose of 0.25 gm. two to four times a day may be administered.

Preparations for use as stated for the foregoing drug are marketed under the following name: Flexin.

McNeil Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of zoxazolamine.
—*J. Am. Med. Assoc.* 162:206 (Sept. 15) 1956.

Preparations

Tablets Zoxazolamine (Flexin) 0.25 Gm., scored.

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

Tuberculosis

Present Status of the Treatment of

COL. JAMES A. WIER (MC), U. S. ARMY.

This report is the seventh in a series[1] by the Veterans Administration-Army-Navy group that has been studying the chemotherapy of tuberculosis since 1946. This report is largely a summary of the data presented at the 15th Conference on the Chemotherapy of Tuberculosis, held in St. Louis, Feb. 6-9, 1956. Its purpose is to briefly summarize data presented as a result of cooperative studies as well as to mention reports of pilot studies and other original work of individual hospitals or investigators. For more details on methods and techniques of the cooperative studies, reports of early conferences or the recent summary by Tucker[2] may be consulted.

This report is directed primarily toward the internist and general practitioner of medicine rather than toward the specialist in pulmonary disease or tuberculosis. No effort will be made to report on all papers presented or to interpret any of the more controversial material debated.

Three Basic Chemotherapeutic Regimens

Comparison has been made of 3,250 cases of pulmonary tuberculosis treated for at least four months with one of the three following regimens: 1 gm. of streptomycin given twice weekly plus 12 gm. of aminosalicylic acid (PAS, formerly para-aminosalicylic acid, U. S. P. XIV) administered daily; 1 gm. of streptomycin given twice weekly plus 0.3 gm. of isoniazid administered daily; or 0.3 gm. of isoniazid plus 12 gm. of aminosalicylic acid administered daily. These regimens, which were assigned to patients by random allocation, were continued for 12 months or longer in most instances. Results have revealed no differences regarding x-ray improvement or bacteriological conversion in patients with minimal pulmonary tuberculosis; however, in patients with far-advanced pulmonary tuberculosis, the bacteriological conversion rate at 5 to 8 months and at 9 to 12 months was significantly better in patients receiving isoniazid plus aminosalicylic acid than in those receiving either streptomycin plus isoniazid or streptomycin plus aminosalicylic acid. In these cases, the streptomycin was administered twice weekly. The streptomycin-isoniazid combination produced slightly better results than the streptomycin-aminosalicylic acid combination in the far-advanced cases. Careful evaluation of results and personal experiences of all investigators supported the belief that roentgenographic improvement per se was the least important means of evaluating results of drug therapy, particularly in more advanced and cavitary disease. It was felt that evaluation of cavity closure and bacteriological conversion and eventual relapse rates would be the most reliable guides.

From the Fitzsimmons Army Hospital, Denver.

THORAZINE* ...*dramatic in emergencies*

vomiting
alcoholism
severe pain
hiccups
acute excitement
status asthmaticus

	Package Size	Price to Hospital
Ampuls 1 cc. 25 mg.	Boxes of 6 Packages of 100 **Packages of 500†**	$3.12 box 44.00 pkg. **195.00 pkg.**
Ampuls 2 cc. 50 mg.	Boxes of 6 Packages of 100 **Packages of 500†**	4.38 box 62.00 pkg. **240.00 pkg.**
Suppositories 25 mg.	Boxes of 6	1.23 box
Suppositories 100 mg.	Boxes of 6	1.53 box
Syrup 10 mg./5 cc.	4 fl. oz. bottles	1.53 each
Tablets 10 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	2.13 each 20.24 each **170.00 each**
Tablets 25 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	3.03 each 28.79 each **243.00 each**
Tablets 50 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	3.63 each 34.20 each **270.00 each**
Tablets 100 mg.	Bottles of 50 Bottles of 500 **Bottles of 5000†**	4.83 each 46.32 each **366.00 each**
Tablets 200 mg.	Bottles of 500 **Bottles of 5000†**	64.85 each **510.00 each**

†Available only to *non-profit* (tax exempt) institutions for use within the institution.

Smith, Kline & French Laboratories, Philadelphia

*T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.

In the evaluation of cavity closure, differences in results with these three regimens were least apparent in patients with small cavities. In patients with cavities no larger than 1 to 2 cm. in diameter, the percentage of cavity closure at 12 months without use of resectional surgery was the same with streptomycin plus isoniazid and isoniazid plus aminosalicylic acid, but only slightly lower with streptomycin plus aminosalicylic acid. In patients with cavities of 2.5 to 3.5 cm., the combination of isoniazid plus aminosalicylic acid was slightly more effective than the other regimens; in patients with cavities larger than 4 cm. in diameter, the isoniazid—aminosalicylic acid combination yielded a significantly higher percentage of cavity closure at 12 months than did the other two regimens. The streptomycin-aminosalicylic acid combination proved least effective. This superiority of isoniazid plus aminosalicylic acid was apparent at each evaluation period.

Bacteriological resistance to streptomycin (equal growth in 10 mcg. per milliliter in vitro) did not differ significantly in the groups treated with streptomycin-isoniazid or streptomycin-aminosalicylic acid. A different picture was presented, however, concerning isoniazid resistance (equal growth in 5 mcg. per milliliter in vitro). There was a significantly higher incidence of patients with organisms resistant to isoniazid when they were treated with streptomycin plus isoniazid than when they were treated with isoniazid plus aminosalicylic acid. This became more apparent at each observation period after four months and was more striking in patients with cavities larger than 4 cm.

In summary, it may be stated that the combination of isoniazid plus aminosalicylic acid was significantly more effective than either of the other two regimens in the treatment of pulmonary tuberculosis, especially in those patients with more advanced disease; in less extensive disease there was no significant difference between the regimens.

Pilot Studies

Triple Drug Therapy.—Two hundred eighty patients were treated for at least eight months with a three-drug combination, streptomycin plus isoniazid plus aminosalicylic acid, as compared to a streptomycin-isoniazid combination or streptomycin plus aminosalicylic acid. Results showed little difference, except that there was more bacteriological conversion at all evaluation points with the first two combinations. The streptomycin was administered twice weekly in all the combinations.

Streptomycin Administration.—Preliminary results in treatment of 142 patients would tend to confirm the British Medical Research Council studies,[3] which demonstrated that administration of 1 gm. of streptomycin plus isoniazid, both given daily, produces less emergence of organisms resistant to isoniazid than administration of 1 gm. of streptomycin twice a week and isoniazid daily.

Duration of Chemotherapy.—Results of cooperative study comparing the effectiveness of treatment in patients receiving 6 or 12 months of drug therapy after achieving x-ray stability, cavity closure, and bacteriological conversion have been inconclusive. All investigators were in general agreement that drug therapy should be continued for at least a year in all cases and for no less than six months after the achievement of clinical control of the disease as defined previously. Chemotherapy of longer duration should be used in patients with more extensive disease and with so-called open-healed cavities.

Bed Rest.—Cooperative studies to evaluate the need for bed rest have been largely inconclusive. One Veterans Administration hospital has treated all patients for several years on a liberal basis of free activity within the hospital. Their results in a group of 200 patients compare favorably with the over-all results reported from other Veterans Administration hospitals. One Army hospital has established a program to evaluate the importance of modified bed rest as compared to ad libitum ambulation in hospitalized patients. A preliminary report indicated no differences in the results in 95 patients on bed-rest therapy and in 80 patients permitted early ambulation. It was emphasized by all concerned that preliminary hospitalization of tuberculosis patients was indicated and initial home care was not recommended, even though it appears feasible to shorten the duration of hospitalization in most patients undergoing original drug treatment.

Individual Drugs

Pyrazinamide.—In 1954, at the 13th Veterans Administration Conference, there had been concern over the use of pyrazinamide because of an apparently high incidence of toxic effects on the liver; however, its effectiveness in animals, where combined with isoniazid, and the results of therapeutic trials in humans, have reawakened more widespread interest in this drug. It has been found that combined pyrazinamide-isoniazid therapy is effective in patients who have never received either drug before. A preliminary report at this conference, on a relatively small number of cases, indicated that this two-drug combination (137 patients treated) was somewhat more effective in bringing about x-ray improvement, bacteriological conversion, and cavity closure than were streptomycin plus isoniazid (78 patients), isoniazid plus aminosalicylic acid (112 patients), or streptomycin plus aminosalicylic acid (115 patients). In all studies reported there is a significant factor of toxic effect on the liver; approximately 10% of the patients receiving pyrazinamide showed abnormal results in liver function tests, and about 3% showed frank jaundice. Most of these conditions, however, revert to normal when the drug is withdrawn. One exception to the reported toxic effect on the liver was in the group of patients previously reported by the Public Health Service, in which the rate of toxicity was much lower. The combination of pyrazinamide plus isoniazid also was effective in patients with organisms resistant to streptomycin and/or aminosalicylic acid. Pyrazinamide alone may be used with reasonable success for periods of 30 to 60 days to cover surgery in patients resistant to other major drugs. Pyrazinamide plus viomycin was believed to produce no better results than those expected with pyrazinamide alone.

Cycloserine.—The effectiveness of cycloserine in the treatment of pulmonary tuberculosis has now been investigated for about two years. A preliminary report on cycloserine alone versus combined isoniazid-aminosalicylic acid therapy has established that cycloserine alone is inferior to this combination in all respects evaluated. Schmidt reported that cycloserine and isoniazid appear to act synergistically against tuberculosis in the monkey. Preliminary clinical reports by Epstein indicate that cycloserine plus isoniazid may be an

Upjohn

diarrhea...

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Each fluidounce contains:
Kaolin . . . . . 90 grs.
Pectin . . . . . 2 grs.
in an aromatized and carminative vehicle
Available in bottles of 6 and 10 fluidounces and 1 gallon

The Upjohn Company, Kalamazoo, Michigan

effective regimen in man. Reports of toxicity, particularly to the central nervous system, have continued. This toxicity appears to be related to blood levels of the drug and is higher with levels over 30 mcg. per milliliter. There has been no indication of increased toxicity from the combined use of cycloserine and isoniazid.

Hinconstarch.—A combination of amithiozone, isoniazid, and starch was studied in experiments with animals. It was felt to be about as effective as the amithiozone and isoniazid contained in the combination might be individually, although there was some indication that the toxicity of amithiozone was lessened in the starch combination.

Isoniazid.—Isoniazid is degraded in human subjects into several derivatives, one of these being biologically inactive acetylisoniazid. It has been shown that the degree of this inactivation may vary significantly from individual to individual. The usual chemical assay method (Poet and Kelly) for determining the isoniazid level in serum does not distinguish between the active free isoniazid and the biologically inactive derivatives. As a consequence, some individuals with adequate serum levels determined by the chemical method will have an entirely inadequate level as determined by the bioassay methods, indicating that in these individuals there should be little therapeutic effect from the isoniazid used. Variations of free isoniazid in the urine reflect the free (biologically active) isoniazid in serum. In some of these individuals the simultaneous administration of aminosalicylic acid will elevate the level of biologically active isoniazid in the serum, probably by competing for the acetylation mechanism.

Thoracic Surgery

Surgical Resection.—Consolidated data presented at the conference indicated that 1,307 pulmonary resections were done during the last year. The percentages of types of operations for 1954-1955 were pneumonectomy, 5%; lobectomy, 39%; and segmental and wedge resection, 56%. Mortality rates for these procedures were pneumonectomy, 21%; lobectomy, 4%; segmental resection, 1.3%; and wedge resection, none. The overall rates of mortality for the period 1953 to 1955 inclusive were pneumonectomy, 16.5%; lobectomy, 3.3%; segmental resection, 1%; and subsegmental resection, none. The rate of serious complication as evidenced by empyema was pneumonectomy, 18.5%; lobectomy, 4.7%; segmental resection, 4%; and subsegmental resection, 0.8%. The incidence of complication is higher in the patient previously treated, but with tubercle bacilli still susceptible to the drugs being used, than in a patient receiving treatment for the first time; complications are most frequent in patients previously treated whose tubercle bacilli are drug resistant.

Resection of Closed Lesions.—One Veterans Administration hospital reported on a follow-up of patients with pulmonary tuberculosis with closed lesions in whom surgical resection or medical treatment was administered by random selection. Four of 43 patients in whom resection of closed lesions was added to medical treatment had relapses; 3 of 56 in whom resection was not done had relapses. In general, an increasing lack of enthusiasm was noted among the investigators for resection of closed necrotic lesions in patients receiving adequate chemotherapy.

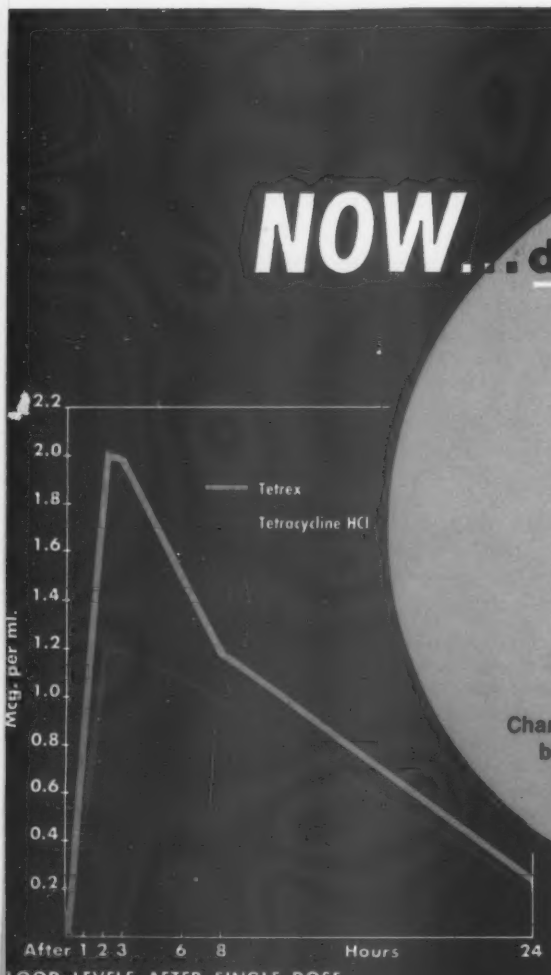

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Chart (left) shows blood levels practically double with Tetrex

— from 3 independent studies by P. A. Bunn, M.D., Sol Katz, M.D., and G. A. Cronk, M.D., on 188 patients

Morphology and Bacteriology of Closed Lesions.—Data from the cooperative study were presented on bacteriological examination of 1,367 surgically resected lesions, of which 64% were closed lesions, 13.5% were open lesions, and 22.5% were mixed. Seventy percent of the closed lesions were negative for tubercle bacilli by culture, whereas 40% of the open and 44% of the mixed lesions were negative. It was noted that, the larger the closed lesion, the higher the percentage of bacteriological positivity; and the longer the period of preoperative chemotherapy, the fewer the number of positive lesions. The duration of preoperative chemotherapy seemed to have no relation to the percentage of positivity of open lesions.

Nonpulmonary Tuberculosis

Miliary and Meningeal Tuberculosis.—The favorable trends noted with miliary and meningeal tuberculosis reported previously are continuing. A two-year follow-up has revealed 95% survival of patients with miliary tuberculosis treated with streptomycin-isoniazid, with or without aminosalicylic acid; the two-year survival rate in patients with meningitis similarly treated is 80%. Most of these patients have received triple therapy, but all have received isoniazid and streptomycin. These results are significantly better than were accomplished previously with a combination of streptomycin and aminosalicylic acid.

Genitourinary Tuberculosis.—One investigator, expanding on the results of chemotherapeutic regimens in genitourinary tuberculosis, indicated that triple therapy has shown about 5% better results than any combination of two drugs. He again emphasized the trend toward less surgical intervention in renal tuberculosis. He recommended that drug therapy for most cases of renal tuberculosis be continued for at least 24 months.

Some Special Problems

The Open-Negative Tuberculous Cavity.—The open-negative tuberculous cavity is defined as an empty space lined by hyalinized connective tissue with no sign of specific inflammation in the wall and with no exudate in the space. Ninety-eight surgically resected cavities were examined. Twelve showed open healing on pathological examination; 55 cavities were active clinically, and on pathological examination 31 were clinically open-healed with negative preoperative bacteriology. Of these clinically open-healed cavities, two-thirds were active on pathological examination. Only 4 of 12 open-healed cavities (pathologically) had typical thin-walled appearance as evidenced by a preoperative x-ray. In some instances, patients with open-healed cavities were treated with streptomycin plus aminosalicylic acid, indicating that this phenomenon is not necessarily the result of treatment with isoniazid as has been suggested.

The in Vitro Action of Antituberculosis Agents Against Multiplying and Nonmultiplying Organisms.—Further evidence was presented that indicated that both streptomycin and isoniazid are most active against tubercle bacilli that are actively multiplying and that they have little effect on those that are not multiplying or are in a resting state.

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Summary

As data accumulate on large numbers of patients with pulmonary tuberculosis treated with long-term combined chemotherapy, it is increasingly evident that most patients undergoing an initial course of therapy do well on any of the adequate drug regimens. Significant differences occur only in patients with far-advanced disease who are selected on the basis of large cavities or multiple bilateral cavities. In these cases the best results have been obtained when isoniazid and aminosalicylic acid are given daily in combined therapy. These findings suggest that no rule of thumb can be dictated that will apply to chemotherapeutic treatment of all patients with pulmonary tuberculosis. In these problem cases, other factors are arising that further complicate the proper treatment of the individual. These include the different rates of inactivation of the chemotherapeutic agent in the patient being treated, the significance of the open cavity remaining in a patient who is always bacteriologically negative, and the development of resistance of the bacterial organisms to the chemotherapeutic agents used.

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LETTERS

National Pharmacy Week Participation

DEAR SIRS: May I congratulate you on your fine publication which is always of great interest to pharmacists and laymen associated with the medical profession.

We are proud of the Pharmacy Department here at the Hospital Center and the role it plays in contributing to higher medical standards and better health for our patients. For that reason, I am enclosing a picture I thought you might like to use in the forthcoming edition of your magazine.

Also, I thought you might be interested in the newspaper feature story released to the local press by our Public Relations Department during National Pharmacy Week. I think you will agree the story gives a true picture of the operational scope of a pharmacy serving a Hospital Center of 377 beds and 58 bassinetts for the new-born.

E. BRENT SNODGRASS,
Public Relations Representative
The Hospital Center at Orange,
Orange, N. J.

EDITORS NOTE: The complete text of the release referred to in the above letter is published on page 580 of this issue of THE BULLETIN. This will serve as an example of a public relations program for hospital pharmacy.

Error in Listing of Internship Programs

DEAR SIRS: Through an error, our hospital was listed in THE BULLETIN (March-April, 1956 issue) as offering an internship program in hospital pharmacy.

The University of Tennessee does offer a Masters' Degree in hospital pharmacy and our hospital cooperates as part of the teaching program. Any information desired as to the graduates of this program can be secured from Mr. Howard Hassler, School of Pharmacy, University of Tennessee.

JOE R. SYKES, *Chief Pharmacist*
John Gaston Hospital
City of Memphis Hospitals
Memphis 3, Tennessee

From Thailand

DEAR SIRS: I want to thank you for all the papers you have sent to me. They are most valuable in my work and I have made use of them often.

Enclosed is five dollars for which I would like to continue my subscription to THE BULLETIN . . .

CHAWEE BUNNAG, *Pharmacist*
School of Pharmacy
University of Medical Sciences
Phyathai Road
Bangkok, Thailand

Appreciation

DEAR SIRS: I am sending this note to thank you for the help given me in connection with securing a position. I recently became Chief Pharmacist at The Staten Island Hospital, Staten Island, N. Y. and I secured the position after being notified of the opening through my note in THE BULLETIN.

Once again, thank you.

SHELDON J. SCHWARTZ, *Chief Pharmacist*
Staten Island Hospital
Staten Island, N. Y.

Appreciation For Help From Division Office

DEAR SIRS: Thank you for your prompt response to my requests in the past. The information has been a help to all of us concerned and I have passed it along to the Chairman of our Pharmacy and Therapeutics Committee. You will be interested to know that we now have a fully organized Pharmacy and Therapeutics Committee and the enthusiasm and cooperation from the members has been most encouraging . . . We have our meetings at 8 A. M. which is usually a good time unless there is emergency surgery or an emergency call.

SISTER M. EMMANUEL, *Chief Pharmacist*
St. Alexius Hospital
Bismark, North Dakota

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EDITORIAL

Audit of Pharmaceutical Service in Hospitals

by Don E. Francke

In January 1957 the first questionnaire of the Audit of Pharmaceutical Service in Hospitals will be mailed to a scientifically selected sample of 3,500 hospitals. Thus, after several months devoted to planning, those working on the Audit are ready to begin that phase of the study concerned with data collection.

The success of this national study of hospital pharmacy practice rests in a large measure with individual hospital pharmacists and particularly with the members of the SOCIETY. Your cooperation is vital. Each hospital pharmacist has a professional responsibility to assist in the survey in every possible way. The greatest single act of cooperation is to conscientiously fill out the questionnaire and return it as soon as possible. Other professional groups have made similar studies to improve their services to patients. All of these studies have had the cooperation of the individual members of the professional groups. We are confident that hospital pharmacists also will extend to this survey of their specialty, their full and whole-hearted enthusiastic support.

This is the first comprehensive, national study of pharmaceutical service in hospitals undertaken in the United States. It is being carried out under the auspices of the Division of Hospital Pharmacy of the A.Ph.A. and the ASHP under a grant of $36,000 from the U.S. Public Health Service. The principal investigator and program director of the research project is Dr. Don E. Francke, while Mr. Clifton J. Latiolais is the assistant director of the study working on a full-time basis. The specialized services of the Survey Research Center of the University of Michigan have been made available and are being utilized in developing methodology, sampling, and other specific areas of the study. The Policy Committee of the Division of Hospital Pharmacy serves as an Advisory Committee to the Audit. A Committee on Hospital Pharmacy Practice has been appointed to assist in planning specific areas of the study.

The basic objectives of the study are to determine what constitutes good pharmaceutical service for patients in hospitals and to study methods of improving and extending this service in the interest of better patient care. In order to accomplish these broad objectives, it is necessary (1) to examine present methods of pharmaceutical practice and service in hospitals; (2) to outline the elements of pharmaceutical service which will promote better patient care; (3) to determine how these elements of service may be more effectively performed for the benefit of the patient, the medical and allied staffs, and the hospital; (4) to consider the education and training desirable for hospital pharmacists to enable them to perform these elements of service, and (5) to recommend a plan of action for the implementation of the findings of the Audit. The need for extending pharmaceutical service to small hospitals is being given particular attention in this study.

Three approaches to the problem are being utilized. These consist of questionnaires directed to pharmacists and, in some cases, to administrators, personal interviews and case studies. The questionnaire will be sent to a scientifically selected sample of general, short-term hospitals with less than 100 beds, to pharmacists in all general short-term hospitals with more than 100 beds, and to pharmacists in a sample of the special long-term hospitals. Personal interviews will be conducted by members of the Audit staff in a subsample of the hospitals selected, and a series of case studies will be done in selected hospitals associated with teaching institutions and in other hospitals from which specialized information is needed.

Once the data has been collected it will be processed and tabulated so that it may be analyzed and a report with recommendations for implementation can be prepared. The successful completion of the Audit will provide factual data which will serve as a basis for improving the quality and scope of pharmaceutical service to patients, establish standards of procedure in keeping with modern hospital practice, and enable better economic planning in the integration of pharmaceutical service with hospital administration and professional services in general.

The successful completion of the Audit of Pharmaceutical Service in Hospitals requires the wholehearted cooperation and active participation of all hospital pharmacists. Officers of Affiliated Chapters of the SOCIETY will be called upon for special assistance and will be contacted soon regarding the role of Affiliated Chapters in the Audit.

ANTISEPTICS

IN THE HOSPITAL PHARMACY

by GEORGE F. REDDISH

ANTISEPTICS ARE OF MUCH IMPORTANCE to the hospital pharmacist, and for many reasons. The different classes of antiseptics employed for various purposes, their relative ratings for these specific uses, the mechanism of action under conditions of application, stability in the presence of organic matter, etc. are all of great interest to the pharmacists who prepare and dispense them for hospital use. There are also other factors which affect the suitability of different classes of antiseptics for various purposes.

Definitions

Although hospital pharmacists are, of course, well informed as to what antiseptics are expected to accomplish when used in practice, it may be useful to repeat here the official definition of the word. Although the word "antiseptic" literally means "against sepsis" or "against infection," the word has sometimes been applied technically to mean substances which merely "inhibit the growth of bacteria." This wholly erroneous definition is still used in some textbooks on bacteriology and in certain published papers on the subject.

It is only necessary to take the original meaning of the word, that is, "against infection," in order to arrive at the proper definition, the one used by the medical, dental, and veterinary professions and by the layman as well. The following definition was first used by the U.S. Food and Drug Administration in the control of antiseptics:

> Antiseptics are substances which, when applied to microorganisms, will render them innocuous either by killing them or preventing their growth, according to the character of the preparation or the method of application. This term is used especially for preparations applied to living tissue.[1]

Presented at the Section on Hospital Pharmacy, 75th Anniversary Meeting of the Wisconsin Pharmaceutical Association, Madison, Wisconsin, June 1, 1955.

GEORGE F. REDDISH, Ph.D. is associated with the St. Louis College of Pharmacy and Allied Sciences and the Lambert-Hudnut Division of Warner-Lambert Pharmaceutical Company, St. Louis, Mo.

Essentially the same definition has been included in the Federal Food, Drug, and Cosmetic Act[2] as follows:

> The representation of a drug, in its labeling, as an antiseptic, shall be considered to be a representation that it is a germicide, except in the case of a drug purporting to be, or represented as, an antiseptic for inhibitory use as a wet dressing, ointment, dusting powder, or such other use as involves prolonged contact with the body.

If a drug acts "against infection," it can do so either by killing infectious microorganisms or by preventing their growth. The most certain means for acting "against infection" is to actually kill the bacteria present. Antiseptics which act in this manner are called germicides. If, on the other hand, a drug is of such a nature, or is used in such a way as to simply prevent the growth of bacteria, and by so doing prevents infection, it can also be classed as an antiseptic. These latter are primarily bacteriostatic agents and are classed as antiseptics because, when used clinically, they act "against infection." It is therefore not difficult, nor is it inconsistent, to give a double meaning to this word. Many English words have double meanings, and the word "antiseptic" is a good example.

Classes of Antiseptics

Antiseptics then, are chemical substances which kill or prevent the growth of microorganisms when applied to living tissue. Some of the more important antiseptics are:

Halogens. Iodine and certain chlorine compounds are widely used as antiseptics. Iodine has been used for the purpose since 1839 and in surgery since 1862. The common forms are: Iodine Tincture, U.S.P., (since 1940) consists of 2.0 percent I, and 2.4 percent NaI in alcohol (U.S.P. XV); Iodine Tincture, Strong, N.F. 7 percent I and 5.0 percent KI in alcohol; Iodine Solution, N.F., 2.0 percent I and 2.4 percent NaI in H_2O. The best is the tincture which penetrates rapidly, is highly germicidal, non-specific, and is not counteracted by organic matter. Chlorine compounds, counteracted to variable extents by organic matter, include sodium hypochlorite (Dakin's solution), dichloramine—T, etc. Fluorine and bromine are effective but not used.

Mercury Compounds. *Inorganic.* Mercuric chloride has been widely used since 1881, but largely replaced by less toxic compounds, whereas mercurous chloride, mercury oxycyanide, mercury cyanide, and potassium mercuric iodide have but limited use. These compounds are bacteriostatic in high dilution, germicidal in much greater concentrations, but counteracted to a large extent by organic matter.

Organic Mercury compounds are far less toxic, non-irritating, and are highly bacteriostatic, germicidal, and non-specific, but counteracted to variable degrees by organic matter; the most important are merphenyl nitrate, Merthiolate, Metaphen Mercurochrome, and Mercresin.

Silver Compounds. The most widely used silver compounds are Silver Nitrate, U.S.P., Ammoniacal Silver Nitrate Solution, N.F., silver picrate, N.N.R., and certain colloidal silver preparations such as Strong Protein Silver, N.F., Mild Silver Protein, U.S.P. (Argyrol), etc., all of which are effective germicides of low toxicity; they are used extensively on mucous membranes and they are not counteracted by organic matter.

Bis-Phenols. These compounds are highly bacteriostatic and fungistatic and are widely used for the purpose, especially in soaps and detergents, mildew preventing formulations, etc., the halogenated form being most commonly employed, such as dichlorophene, tetrachlorophene, hexachlorophene, and bithionol. The germicidal properties are considerably reduced in the presence of organic matter. When used repeatedly on the skin, as in soaps and detergents, they have a tendency to remain for long periods, thus reducing skin bacteria to a significant degree, hence valuable in preoperative hand washing.

Phenolic Compounds. While phenol was the first widely used antiseptic, employed from 1865 to 1880 and later, it has been largely replaced because of its highly toxic property. Certain compounds, such as Saponated Cresol Solution, N.F., and halogenated phenol derivatives and others, are effective for the purpose, are less toxic and not counteracted appreciably by organic matter.

Quaternary Ammonium Compounds. Many organic pentavalent nitrogen compounds are germicides. While these are used primarily as disinfectants, a few are employed as antiseptics, such as in Zephiran, Cepacol, etc. They are effective for the purpose in proper concentration, but are counteracted to an appreciable extent by organic matter, especially by blood serum. They are, however, non-toxic and non-irritating, and may be used in the place of alcohol following preoperative scrub-up.

Essential Oils. These volatile oils, both natural and synthetic, have been used as antiseptics for centuries and are still widely employed for this purpose. The most important are thymol, eucalyptol, menthol, bergamot, etc. In the concentrations used these oils are effectively germicidal, non-toxic, non-irritating, agreeable as to taste and odor, and not counteracted by organic matter.

ALCOHOLS. Used effectively since 1894, alcohols are still widely employed as antiseptics. Ethyl alcohol in 62.5 percent to 70 percent concentration is most commonly used. It is rapidly germicidal, but weakly bacteriostatic in higher dilution, is non-toxic, non-irritating, and not counteracted by organic matter; it is widely used for degerming the skin. Isopropyl alcohol is equal if not superior to ethyl alcohol, but methyl alcohol is much weaker.

OXIDIZING COMPOUNDS. For certain purposes oxidizing compounds are effective antiseptics. The most important are hydrogen peroxide, zinc peroxide, potassium permanganate, sodium perborate, and glycerite of peroxide. Because of danger associated with the use of these compounds, they are usually employed for special purposes, especially where large amounts of organic matter are not present.

DYES. Bacteriostatic dyes have limited and special uses in surgery and are not ordinarily employed otherwise. They are selective in their activity and are used to prevent the growth of specific kinds or classes of bacteria; they are also to some extent toxic to tissue, but not appreciably affected by organic matter. The most important are crystal violet, acriflavine, methylene blue, and the pyridine compounds.

Methods of Testing

Before discussing the more important antiseptics used in hospitals at the present time, it may be useful to refer briefly to the *in vitro* and *in vivo* tests employed for determining the potential clinical value of such drugs. Hospital pharmacists should have a general understanding of the laboratory methods of testing antiseptics and interpretation of the results obtained. Since antiseptics differ considerably in chemical properties and in purposes for which they are employed, methods of testing differ accordingly.

It must first be understood that the phenol coefficient method should never be employed for testing antiseptics. This is a test for *disinfectants* exclusively and *only* for those compounds chemically related to phenol and which act against bacteria in a manner similar to phenol. In testing antiseptics, phenol is used only for determining the resistance of test cultures for which there are well-established standards. No reference to nor comparison with phenol is employed in testing antiseptics. Present methods of testing are designed to determine antiseptic properties under exaggerated conditions of test or which simulate to some degree the conditions under which they are used, with no reference whatever to the effect of phenol under the same conditions as would be expressed by a phenol-coefficient. However, it is useful to know whether or not an antiseptic is equal to a dilution of phenol of known clinical value and this is determined by a standard laboratory test.

LIQUID ANTISEPTICS. Since 2.0 percent phenol had for many years proved effective as an antiseptic, the test for liquid antiseptics was designed to fit this germicide of proved merit. Also, since antiseptics are used to prevent wound infections, it was logical to require them to kill the most common cause of such infections, namely, *M. pyogenes* var. *aureus*. Then, as a factor of safety the test was so designed that products were required to kill very large numbers of this infectious organisms, far more than would be present in wounds, abrasions, cuts, etc.

This method of test makes use of a strain of *M. pyogenes* var *aureus* (No. 209) which is representative of resistant staphylococci freshly isolated from suppurative infections.[3] The formula of the media employed was designed to maintain this resistance. The effect of peptone on the resistance of the test organism was emphasized and the particular brand used as specified. The details of the method of test were set forth[4] and this method has become known as the U.S. Food and Drug Administration Method for testing liquid antiseptics.

Although there are but few bacteria per square centimeter of skin, and only about 10 to 15 million bacteria per ml. of saliva, this test for liquid antiseptics requires the use of 350 million of the most resistant of all skin and mouth bacteria. Since this excessive number of staphylococci must be killed by liquid antiseptics within 5 minutes, it is evident that an adequate margin of safety has been provided. Since 2 percent phenol is so generally recognized as effective when used in practice, antiseptics are required to be germicidally equivalent to 2 percent phenol. The test, therefore, classifies antiseptics as those that are at least equal to 2 percent phenol and those that are not. In other words, products which pass this test may be considered antiseptic. (For details of the test see "Antiseptics, Disinfectants, Fungicides, and Chemical and Physical Sterilization," edited by G. F. Reddish, Lea & Febiger, Philadelphia, 1954.)

GERMICIDAL SPECTRUM. Recently an effort has been made to determine the germicidal spectrum of various kinds of liquid antiseptics against a variety of test organisms.[5] Fourteen microorganisms, of pathogenic or potentially pathogenic species, are used for the purpose. Cultures are grown in 2 percent trypticase and after exposure

to various dilution of antiseptics are subcultured into U.S.P. liquid thioglycollate medium.

Results of these tests show wide variations in resistance of different species of the same test organisms and also between the various classes of bacteria. It is evident from results obtained that the resistance of test organisms must be determined before they are employed in laboratory tests on germicides. Also, it is shown that it is desirable to use a variety of such test cultures in order to obtain a full bacterial spectrum. This test should, by all means, be included in studies of the germicidal activity of antiseptics.

Antiseptic Ointments, Wet Dressings, Dyes, Powders, Oils, etc. These antiseptics must be tested by a method which determines penetration and bacteriostatic activity, and therefore is quite different from the above tests for liquid antiseptics, since they exert their effect over long periods of time. The test is known as the Serum-Agar Cup Plate Method in which the antiseptic is applied directly to the medium containing *M. pyogenes* var. *aureus* of standard resistance.[4,6]

If the preparation tested is antiseptic, a zone of clear agar will surround the cup in which the antiseptic had been placed, and the clear zone will indicate the penetration and bacteriostatic activity of the antiseptic. The test also indicates whether or not the antiseptic ingredient is counteracted by organic matter, in this test blood serum. The size of zone of penetration and bacteriostatic activity by this test has a direct bearing on potential clinical effectiveness. Here again comparison is made with antiseptics of known clinical value.

Reduction of Skin Bacteria. Price [7,8] has developed a very satisfactory method of determining reductions of bacteria on the skin. While this test was designed originally for determining the value of soap in surgical scrub-up for the removal of bacteria from the skin, it is applicable also for evaluating the effectiveness of germicides recommended for the same purpose. It is the best and most accurate method available for the purpose and is especially suitable for testing antiseptic soaps and detergents recommended for the purpose.

The technique follows closely the preoperative scrub-up procedure employed in hospitals. Plate counts are made before and at specified time periods after the use of soap, medicated or non-medicated, or alcohol and other germicides employed after the scrub-up procedure. Care must be exercised and special precautions taken to avoid bacteriostatic action when certain germicides are used. This is essentially a practical test in which only the normal skin flora is involved.

Antiseptics Used in Hospitals

Although there are a large number of effective antiseptics of various kinds, only those currently used by hospital staffs and prepared and dispensed by hospital pharmacies will be considered. This means that many antiseptics available in drug stores will not be discussed. The number of antiseptics considered will therefore be quite limited and will not reflect the large list of effective preparations available.

It will be convenient to discuss these hospital antiseptics somewhat in the order as they are listed above. Since the various departments in different hospitals exercise their prerogatives in the choice or choices of antiseptics employed, there is as a result no uniformity in this regard. Also some departments use old established germicides which have been proved effective by years of clinical experience, whereas others have discarded these in favor of newer preparations recommended for the purpose. This being the case, it may be quite impossible to state categorically which antiseptic is best for each purpose since in many instances the old germicides may be just as good or better than some of the new. That is, the matter of choice is not always based on the germicidal merits of each individual antiseptic, but on certain preferences based on other properties. Also a certain antiseptic may have a wide margin of safety in its germicidal properties as compared to another with a narrow margin of safety and yet both may be equally effective in clinical practice. It is for this reason that it becomes necessary to consider each antiseptic on its individual merits. This is complicated by the fact that some are more suitable for certain purposes than others and vice versa. It will be inadvisable to list these antiseptics as best, second best, etc, for reasons just given, and therefore no effort will be made to classify them in the relative order of their effectiveness.

Halogens. Of the halogens, all of which are germicidal, only iodine is widely used at this time in hospital practice. Chlorine compounds are used for certain purposes, but not ordinarily in hospitals, the most common being sodium hypochlorite, chloramines, dichloramine-T, etc. Fluorine and bromine, while actively germicidal, are highly irritating and possess no advantages over chlorine and iodine.

Iodine as a germicide has been employed for nearly a century as one of the best and most widely used antiseptics in hospitals, as well as for general purposes. Although tincture of iodine was admitted to the *U.S. Pharmacopeia* in 1830 and the compound tincture in 1840, it was not

widely used in surgery until after 1860, with renewed interest for preoperative skin preparation beginning in 1905. Since that time it has been considered a standard antiseptic for use in hospitals throughout the world.

At the present time Tincture of Iodine U.S.P. contains 2 percent I and 2.4 percent sodium iodide in dilute alcohol and Strong Iodine Tincture N.F. 7 percent I and 5 percent KI in alcohol. These concentrations of iodine in alcohol far exceed the actual requirements of a germicidal solution. For this reason these iodine tinctures possess a wide margin of safety as regards bactericidal activity and effectiveness in clinical practice. This is an advantage not often recognized, but for obvious reasons is of considerable importance, especially in surgery and other hospital uses.

The bactericidal efficiency of iodine solutions depends on the concentration of free iodine and is effective over a wide pH range. One of the principal advantages of free iodine in solution is that its germicidal activity against different pathogenic microorganisms does not vary greatly, it even destroys the tubercle bacillus, pathogenic fungi, viruses, and even bacterial and fungous spores in proper concentration. It is of interest to note that the bactericidal properties of iodine solutions are surprisingly constant under widely different test conditions, even in the presence of organic matter. It is non-specific in its activity against the various pathogenic microorganisms under a variety of exaggerated test conditions, an advantage of considerable importance in hospital practice.

The effectiveness of iodine solutions, especially the tinctures, has been established by clinical experience over a period of almost a century. It would be redundant and actually quite unnecessary to present factual data in support of this general conclusion since the value of iodine in clinical practice is well established and widely recognized. It may be of interest, however, to list some of the uses of iodine solutions as employed in hospitals at the present time.

Since the bactericidal efficiency of iodine solutions depends on the concentrations of free iodine present, it is of interest to note that 0.02 percent of free iodine in solution is germicidal within 1 minute by standard *in vitro* test against a variety of pathogenic microorganisms, including the resistant *Micrococcus pyogenes* var. *aureus*.[9] However, the lowest concentration ordinarily used in hospital practice is 2 percent (Iodine Tincture, U.S.P.), which is 100 times the germicidal concentration as determined by a severe laboratory test (F.D.A. method). This margin of safety is desirable, of course, and is one reason why Iodine Tincture U.S.P. has proved so effective in clinical practice.

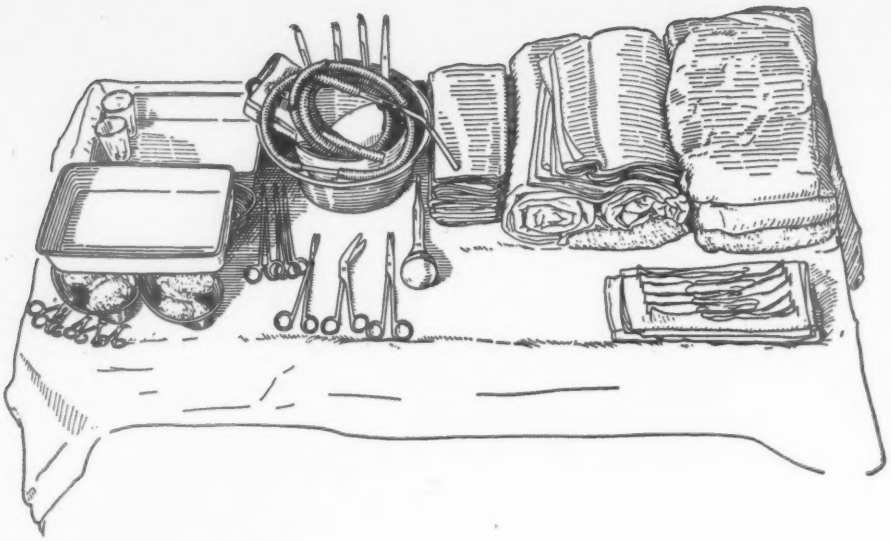
The principal use of iodine solutions in hospitals is as pre-operative skin antiseptics. For this purpose Iodine Tincture U.S.P. (2.0 percent I and 2.4 percent NaI in 47 (44 to 50) percent alcohol) and 3.5 percent tincture are most commonly used. Since the tinctures have low surface tensions (U. S.P.=32.0 dynes) they penetrate into the skin layers and destroy not only the surface transient bacteria, but also the resident bacterial flora within the layers of the skin. Although the tinctures have been most widely used for the purpose over a period of at least fifty years, and found to be eminently satisfactory, the aqueous solution has been employed with success.

Iodine Solution N.F. (2.0 percent I and 2.4 percent NaI in H_2O) has been used satisfactorily as a pre-operative skin antiseptic in a large number of cases.[10] In fact, more than twenty years ago aqueous solutions were highly recommended for the purpose[11] and since then other investigators [12,13] have proved water solutions of iodine one of the most effective germicides available for pre-operative application and general hospital use. Although the tincture has been widely and successfully employed for many years, reports on the effectiveness of aqueous solutions have proved that for pre-operative skin preparations the water solutions have certain advantages.[14]

It is apparent that both alcoholic and aqueous solutions of iodine are effective antiseptics for use on the skin. Both are highly and rapidly effective and, according to a recent report[15], kill all skin bacteria tested within 30 seconds under *in vivo* conditions by a special test. After preparing and cleansing the field of operation, the 2 percent iodine solution is swabbed vigorously on the skin and allowed to remain 2 minutes. If rubbing is not desirable, the solution should be applied and kept moist for 5 minutes, or applied as a wet dressing for this period of time, and the excess removed with 70 percent alcohol. Such skin preparation has been proved both effective and safe.

While iodine solutions are employed in hospitals primarily for pre-operative skin preparation, there are other uses which may be mentioned. In addition to general use in first aid, iodine solutions are quite effective for disinfecting clinical thermometers.[16,17] The disinfecting of drinking water, sanitizing eating and drinking utensils,[16,18] cold sterilization of certain surgical instruments, the treatment of certain fungous infections, etc. are a few of the uses that may be made of iodine solutions in hospitals.

It seems to me that if I were responsible for



getting my hospital in position to serve the nation during a national emergency, such as a bombing attack, I would make sure that I had *good* stocks of two chemicals—*iodine* and *sodium* or *potassium iodide*. With these two straight chemicals on hand, I could make solutions that are known to be effective for many uses, including:

1. Preparation of skin for surgery.
2. Treatment of wounds; washing out of wounds with dilute solutions.
3. Disinfection of surgeons' and nurses' hands and gloves.
4. Emergency disinfection of instruments.
5. Disinfection of clinical thermometers.
6. Disinfection of drinking water.
7. Sanitation of eating and drinking utensils.
8. Therapeutic applications.

I know of no other straight chemicals which can be stockpiled so easily, and which can serve in so many ways, particularly under emergency conditions.

MERCURY COMPOUNDS. Although certain mercury salts had been used to some extent for centuries in the prevention and treatment of infection in open wounds, it was not until the germ theory of disease was fully established that they became widely used for the purpose. After Koch in 1881 proved the germicidal property of mercuric chloride, the medical profession employed this antiseptic in surgery and general practice. It is still used to some extent by the professions and laymen, but has been largely superceded by organic mercurials and others. While the inorganic mercurials are highly bacteriostatic, they are not as germicidal as the organic compounds, which are also less toxic and less irritating, and do not corrode metals.

Because of the more favorable properties of organic mercurials, they have largely replaced mercuric chloride in clinical practice. Several such compounds have been developed during the past thirty-five years, most of which have been employed successfully in practice. A list of mercury compounds and their formulas and germicidal properties has been prepared by Brewer.[19] Although some of these compounds are not widely used in hospitals, it will be of interest to discuss those now generally employed in surgery.

The organic mercurials were first introduced in 1919 by Young et al.[20] who developed Mercurochrome (Merbromin Solution N.F.), solutions of which were later developed for general surgical use (Surgical Merbromin Solution N.F.). According to the Council on Pharmacy and Chemistry of the American Medical Association in its 1950 N.N.R. Merbromin Solution N.F. (2 percent aqueous) is non-irritating, moderately active antiseptic and when used on the skin, mucous membranes, and wounds exerts bacteriostatic action. It acts more slowly than iodine tincture, but has more prolonged bacteriostatic effect. However, Surgical Merbromin Solution N.F. (2 percent aqueous-alcohol-acetone solution) is a more active antiseptic and may be used for preoperative skin preparation, and has been widely and successfully used for the purpose.

Metaphen (Nitromersol Solution and Nitromersol Tincture N.F.) was developed in 1923[21] as a new organic mercurial for general professional use. *New and Nonofficial Remedies* (1950) states that Nitromersol Solution is non-irritating, non-toxic, and without deleterious action on metal instruments or rubber, is used for treating certain

infections, for disinfection of skin, surgical instruments, and rubber. It is usually employed in 1-500, 1-1,000 and 1-5,000 concentrations as a germicide for instruments and skin application.

Phenyl mercuric nitrate, prepared in 1931[22] as a disinfectant is used primarily on inanimate objects and as a preservative and antifungal agent. The phenyl mercuric compounds have not been widely used as antiseptics and are not usually employed as such in hospitals.

Merthiolate (Thimerosal N.F.) was selected from a group of organic mercurial compounds in 1931 and its antiseptic properties evaluated.[23] According to N.N.R. (1950), Merthiolate is bacteriostatic and fungistatic, and in 1-10,000 dilution is effective as a preservative for biologicals, but not necessarily stored liquid plasma in this concentration. It is also used for disinfecting tissue surfaces in proper concentration.

The use of Merthiolate as a skin disinfectant was studied in 1932,[24] and has been widely used for the purpose since. Merthiolate Tincture, 1-1,000 in alcohol-acetone-aqueous solution is used and in many hospitals is employed as the preoperative skin antiseptic of choice. It is rapidly germicidal on the cleansed skin and has the further advantage in that it is not irritating and does not require removal. It also contains a harmless coloring material so that the area of application is clearly outlined.

The advantages of Merthiolate may be briefly stated as follows: (1) It is highly *germicidal* in both aqueous and alcohol-acetone-aqueous solutions, not only in the presence of body fluids, but under other conditions of clinical use; (2) it has the further property of *sustained* antiseptic action and exerts non-specific antibacterial activity long after it is applied; (3) it is highly bacteriostatic even in high dilution which is clinically desirable since dilution often occurs in clinical application; (4) it penetrates even in the presence of blood serum; (5) it is compatible with body fluids in which its germicidal properties are maintained; (6) it is one of the least toxic of the antiseptics and in the dilutions used in practice is harmless to body tissues; and (7) it is non-irritating in such concentrations even when applied as a dressing. It is evident that as a topical antiseptic Merthiolate meets all the requirements for clinical use.

Quaternary Ammonium Compounds. Of the quaternary ammonium compounds, Zephiran is most widely used as an antiseptic, at least in hospitals. For this purpose benzalkonium (Zephiran) chloride tincture 1-1,000 is generally employed. In addition to its excellent germicidal properties, it is also a detergent and, because of the concentrations of alcohol, has a low surface tension which enhances its penetrative properties.

Zephiran is germicidal in high dilution also, from 1-35,000 to 1-95,000 at 37°C, based on the pure anhydrous active ingredient.[25] It is also highly bacteriostatic, inhibiting the growth of pathogenic microorganisms in dilutions up to 1-800,000,[26] again based on the pure ingredient. In addition it is also fungicidal and fungistatic against pathogenic fungi.[25] The rapidity of the germicidal action of Zephiran chloride, even in the presence of blood serum, has been demonstrated.[27] On account of these important properties, Zephiran chloride tincture 1-1,000 is widely used in hospitals, especially in preoperative skin preparation and as a germicidal rinse in surgical disinfection of the hands after scrub-up with soap and water. At the present time Zephiran tincture is used primarily for these two purposes and with very satisfactory clinical results.

Zephiran has been proved to be non-irritating to skin and mucous membranes by both repeated patch tests and by repeated application to the arms and hands as a scrub-up rinse.[28] In surgery the 1-1,000 tincture has been demonstrated to be effective in preventing surgical infections in large series of cases and is now widely used for the purpose. In some hospitals it is the preoperative antiseptic of choice in general surgery, while in others it is preferred in certain departments only, such as obstetrics and gynecology, ophthalmology, etc.

It is also employed in treating certain infections, such as genito-urinary infections, superficial wounds, traumatic injuries, and as a first aid prophylactic, burns, etc. The concentration of Zephiran chloride for these purposes ranges from 1-1,000 to 1-5,000 tincture according to the nature of the infection.

In most hospitals it is also employed as a disinfectant for sharp edge surgical instruments, rubber gloves, sterile storage of instruments, clinical thermometers, etc. For this purpose, 1-1,000 to 1-5,000 aqueous solutions are employed, usually with sodium carbonate and sodium nitrite to prevent rusting. Soap should be removed after cleaning and before application of Zephiran to prevent counteracting its germicidal activity.

Zephiran chloride in either aqueous solution or tincture is therefore considered satisfactory and effective for hospital antiseptic and disinfectant uses.

Bis-Phenols. Of the few bis-phenols at present available for use in hospital practice, only two are generally employed at this time. These are hexachlorophene (G-11) and bithionol (Actamer). These compounds are quite similar in

their antibacterial properties and may well be considered together. Since G-11 has been available for several years and has become established for certain specific uses in most hospitals, whereas Actamer was developed only recently, most of the experience with this class of compounds has been with hexachlorophene. This being the case it will be simpler to discuss the value of G-11 as representative of the group.

All of the bis-phenols have the common property of being highly bacteriostatic and fungistatic and to a lesser degree bactericidal and fungicidal. They are also only slightly soluble in water and require special solvents in formulations for practical use. In addition they are in varying degrees adversely affected by organic matter, and they are similar in certain other respects as well.

The principal, if not the only, use of bis-phenols in hospital practice at the present time is as antibacterial agent in soaps and detergents for use in pre-operative scrub-up. Considerable research has been conducted on this use of these compounds. Suitable methods have been developed for the purpose and results of carefully controlled tests have been published. In addition to strictly laboratory or *in vitro* tests, extensive studies have been conducted on the effects of such medicated soaps and detergents on skin bacteria when used in practice, that is performance *in vivo* tests.

Since the activity of G-11 and Actamer are comparable in both soap and detergent, it is possible to illustrate the activity of both by describing the use and effectiveness of a single formulation. For this purpose Septisol, an antiseptic liquid soap widely used in hospitals, will serve the purpose. By antiseptic, in connection with bis-phenols generally and Septisol as well, is meant primarily bacteriostatic activity and to a lesser degree actual germicidal property. Because of a unique property of G-11, and Actamer as well, prolonged bacteriostatic activity from repeated use on the skin results in an antibacterial effect comparable to reductions of skin bacteria resulting from a single use of a quick-acting germicide.

Skin bacteria are divided into two general classes designated as the "transient" and the "resident" flora. Both groups contain pathogenic bacteria which are responsible for skin and surgical infections. The transient flora can be largely removed mechanically by washing with plain unmedicated soaps and detergents, although neither are effective antiseptics, that are of little if any bactericidal value.[29] While the transient flora which are present on the surface of the skin are removed by soap to some extent, the resident flora, being present in the deeper layers of the skin, are not reduced by such mechanical cleansing. Since staphylococci and streptococci constitute the major members of both flora, it becomes a matter of necessity to reduce their numbers to safe levels by system of pre-operative skin preparation, especially in the scrub-up procedure.

This can be done by the repeated and frequent use of a soap medicated with a bis-phenol such as Septisol, which contains hexachlorophene (G-11). Using a well-known reliable method for determining reduction of bacteria from the skin, it has been proved that 2 percent G-11 definitely reduces the numbers of skin bacteria to a significant degree, both the transient and resident flora, as long as the medicated soap is repeatedly used to the exclusion of other cleansing agents.[30] In fact it has been proved that such repeated uses of G-11 soap on the hands and arms reduce the numbers of skin bacteria considerably below that resulting from conventional scrub procedures.[31]

As a result of repeated and frequent use of G-11 soap on the hands and arms, low counts of skin bacteria are maintained due to the residual antiseptic effect of G-11 remaining on the skin. For this purpose liquid soap containing G-11 has been proved more effect than G-11 in bar soap and is retained on the skin to a greater extent. Septisol, representing this class of antiseptic soap, accomplishes such a reduction of skin bacteria, which is maintained when this medicated soap is repeatedly and frequently used many times each day. As a result, a substantial reduction in the time of surgical scrub-up is possible, with shortening or even elimination of prolonged brush scrubbing, and reduction or elimination of antiseptic rinses following. It must be emphasized that in order to obtain best results liquid soap containing G-11 should be used exclusively and many times daily. Such practice results in a saving of time and materials in the pre-operative scrub-up preparation. The skin is not in any sense rendered germ free, but the numbers of skin bacteria are reduced to safe levels comparable to that following conventional scrub procedure.

Recent studies on the use of antiseptic Septisol in pre-operative scrub-up tests have shown that when used daily, six-minute periods on each day, substantial and significant reductions in skin bacteria are shown after the second day. These reductions compare favorably with reductions of skin bacteria following conventional scrub procedure, and, in fact, in all instances the bacterial reductions were greater following the use of antiseptic Septisol than resulted from conventional scrub. The results of these tests are shown in the following table.

DETERMINATIONS OF BACTERIAL COUNT[a]

	PRIOR TO SCRUB	IMMEDIATELY AFTER SCRUB	2 HOURS AFTER SCRUB
Conventional Scrub Standard hospital scrub-up technique with ordinary liquid soap, brush, and antiseptic rinse (10 minutes). Average of 4 subjects in 5 daily scrubs.	2,737,000	400,000	1,258,000
Procedure A (10-minute wash) Antiseptic Septisol without brush or antiseptic rinse. Average of 16 subjects in first use.	2,660,000	375,000	894,000[b]
Procedure B (6-minute wash) Antiseptic Septisol without brush or antiseptic rinse. Average of 4 subjects.			
First Day	3,767,000	1,250,000	477,000
Second day	1,059,000	378,000	338,000
Average (after 2 days' use)	561,000	68,000	182,000
Procedure C (3½-minute wash) Antiseptic Septisol without brush or antiseptic rinse. Average of 7 subjects.			
First Day	1,748,000[c]	1,102,000	206,000
Second day	756,000	269,000	296,000
Average (after 2 days' use)	554,000	234,000	378,000

a. All determinations of bacterial count were made with a neutral liquid soap without G-11.
b. 24 hours after scrub.
c. The low value of this preliminary count is explained by the fact that 4 of the subjects used G-11 soaps in a series of the preceding week.

Results—The same subjects employed in the conventional scrub determinations performed a series of 5 consecutive daily scrubs according to the above 6-minute Procedure B. It is noteworthy that, under these conditions of *single daily exposure,* the bacterial level achieved after the second daily wash is comparable to the conventional scrub and quite superior with continued daily use. After the first day the bacterial levels before, and two hours after the scrub, are significantly lower than in the conventional scrub series when ordinary soap was used, illustrating the residual effect of Antiseptic Septisol.

ALCOHOLS. Alcohol is one of the oldest and most widely used of the skin antiseptics, especially during the past sixty years. For many years ethyl alcohol only was used for the purpose, but recently isopropyl alcohol has been employed rather widely. Both are effective in destroying pathogenic bacteria present on the skin and to some extent within the superficial skin layers.

For this purpose 70 percent alcohol is generally employed. It is of interest to note that alcohol begins to be germicidal against the resistant staphylococci in 40 percent concentration and is active against these microorganisms up to 90 percent, and then is less effective in 95 percent and 100 percent concentration, especially if the bacteria are dry. By standard test 40 percent alcohol is germicidal against staphylococci within 4 minutes, 50 percent in 30 seconds, and 60 percent within 10 seconds.[32] The medical departments of some of the U. S. military services recommend the use of 62.5 percent alcohol for use as a skin antiseptic and have proved it just as effective as 70 percent or higher concentrations.

Although it is practically impossible to sterilize the skin, such use of alcohol reduces the number of skin pathogenes to safe levels. While this has been proved by over a half century of clinical experience, recent confirmation of its effectiveness has been reported[33,34,35]. It is evident that alcohol in suitable concentration is effective as a skin antiseptic and its wide use for the purpose is justified.

Ethyl and isopropyl alcohols in 70 percent concentration are also used for disinfecting surgical instruments in combination with certain other germicides. They are also employed for the disinfection of clinical thermometers, for which purpose they are eminently satisfactory. For this purpose 70 percent ethyl alcohol has been proved superior to most of the other germicides recom-

mended with the exception of alcoholic solutions of iodine and the tincture of two of the quaternaries 1-1,000.[36] Even resistant tubercle bacilli are killed by 70 percent alcohol, as well as diphtheria bacilli, staphylococci, streptococci, etc. Immersion of the thermometers in 70 percent alcohol for 10 minutes is sufficient for the purpose.

Other Antiseptics Used In Hospitals

Certain other antiseptics are also employed in hospitals, some of them routinely and others for special purposes. It may be useful to simply mention a few of those that the hospital pharmacist must keep in stock or be prepared to formulate at any time.

Silver Compounds. Of the silver compounds, the most widely used are silver nitrate solution, ammoniacal silver nitrate solution, silver picrate, and certain of the colloidal preparations such as some of the proteinates, for example mild silver protein (Argyrol), etc. These are used primarily on mucous membranes such as for prophylaxis of ophthalmia neonatorum, conjunctivitis, nose and throat applications, gynecologic practice, etc. Such preparations are non-irritating, bland, and especially suited for such uses.

Phenolic Compounds. Although phenol was employed as an antiseptic for many years following its use by Lister in antiseptic surgery, it has been almost completely replaced by certain of the halogenated phenol derivatives, which are more effective germicides, are less toxic, and not counteracted appreciably by organic matter. Although used primarily as disinfectants, many phenol derivatives are useful as antiseptics, such as compounds containing o-phenyl phenol ("O-syl"), resorcinols, chlorothymol, picric acid, etc. These have special uses and are effective as antiseptics for certain purposes.

Essential Oils. Certain volatile oils, both natural and synthetic, are employed to some extent in hospitals, thymol and related oils being most useful. They are effectively germicidal, nontoxic, non-irritating in proper concentration, and not counteracted by organic matter.

Oxidizing Compounds. While certain of the oxidizing compounds are antiseptic, they are not generally used at this time. Some of them, such as hydrogen peroxide, zinc peroxide, potassium permanganate, sodium perborate, and glycerite of peroxide are sometimes employed for special purposes.

Dyes. Bacteriostatic dyes, while formerly employed for special purposes, are not widely used at present. They are selective in their antiseptic action and are not appreciably affected by organic matter. Crystal violet, acriflavine, and the pyridine compounds are representative of this group.

Evaluation of Surgical Antiseptics

The evaluation of surgical antiseptics depends, of course, on specific applications; some antiseptics are suitable for certain purposes and not for others. Therefore it is difficult if not impossible to list them in the order of their effectiveness or value for general surgical use. It is necessary to classify them in separate categories and then attempt to evaluate them on their respective merits. In the last analysis clinical effectiveness is the final criterion. Although surgeons have individual preferences and consider their respective choices as superior to other antiseptics available to them, a proper evaluation must be based on published reports covering an extended period of time and by different authorities.

The usual procedure in evaluating surgical antiseptics is first to determine its germicidal properties by *in vitro* laboratory tests against a variety of different infectious bacteria under severe, exaggerated conditions of test. This should then be followed by performance tests *in vivo* under practical conditions of use. If the antiseptics give favorable results by both kinds of tests, they are then submitted to clinical trial under actual conditions of use. Then effectiveness as determined by extensive clinical experience is required before such antiseptics are considered satisfactory for routine general hospital practice.

The surgical antiseptics of most importance are iodine, mercurials, quaternary ammonium compounds, bis-phenols, and alcohol. All of these in proper concentration in solutions are actively and rapidly germicidal against all infectious bacteria met with in surgical practice as determined by severe and exaggerated laboratory tests. As an additional margin of safety these antiseptics are used in concentrations greater than the minimum required to pass these tests, and in most instances manyfold, so that when used in surgery the maximum effectiveness is assured.

The most satisfactory *in vivo* performance test for skin antiseptics is the serial basin handwashing test.[37] By this test the hands and arms show resident bacterial counts ranging from approximate 10,000,000 to 70,000,000 in different individuals. Since it is practically impossible to kill all these bacteria on and in the skin, it is of interest to compare the degree of reduction in numbers resulting from application of these surgical antiseptics. Comparative figures can be obtained which are useful in selecting antiseptics for use in surgical practice.

For example, using ordinary scrubbing with brush, soap, and water as a control it is possible to compare the effectiveness of antiseptics for "degerming" the skin. It has been shown by this test

for example, that washing the hands and arms for 2 minutes with tincture of Zephiran causes a reduction in skin bacteria equivalent to that following many minutes of scrubbing. Also that 70 percent to 80 percent alcohol reduce the bacterial flora approximately 90 percent; whereas 50 percent alcohol reduces it 70 percent; 40 percent alcohol reduces it 45 percent, etc.[6] This information is valuable in selecting a germicidal rinse for use in pre-operative scrub-up.

Iodine Solutions. Using the same technique, iodine solutions have been proved most effective for destroying skin bacteria when applied as is customary at the site of operation. The efficiency of iodine solutions for this purpose are as follows, in the order of their effectiveness: 7 percent tincture, 5 percent aqueous (Lugol's), 2 percent tincture, and 1 percent tincture. When applied for 2 minutes to the skin, the following approximate bacterial reductions were obtained: 7 percent tincture, 100 percent; 5 percent aqueous, 99.5 percent; 1 percent tincture, 94.5 percent; as compared with 70 percent alcohol, 88 percent.[38] Because of objectionable features of 7 percent tincture and 5 percent aqueous solutions, the 2 percent tincture is recommended as the iodine solution of choice for the purpose.

Zephiran Solutions. When Zephiran solutions are submitted to the same test, they have been proved less effective than iodine solutions as skin antiseptics in reducing the numbers of skin bacteria. The efficiency of Zephiran solutions under the conditions of this test were as follows, in the order of their effectiveness: 1-1,000 tincture of Zephiran after thorough removal of soap; 1-1,000 tincture of Zephiran after superficial rinsing of soap suds; 50 percent alcohol—10 percent acetone alone; 1-1,000 aqueous Zephiran after thorough removal of soap; and 1-1,000 aqueous Zephiran after superficial rinsing of soap suds.[38] For this purpose the use of 1-1,000 tincture of Zephiran after thorough rinsing to remove soap is recommended.

Mercurials. By this test the mercurials are far less effective as skin antiseptics than either iodine or Zephiran solutions. Under the conditions of this test the efficiency of alcoholic—acetone solutions in reducing skin bacteria was reported as follows,

Reduction of Skin Bacteria as Determined by the Serial-Basin Method of Test

Antiseptic	Time Period of Contact	Percent Reduction of Skin Bacteria*
7% tincture of iodine	30 seconds	100%
5% aqueous iodine	2 minutes	99.5%
2% tincture of iodine	2 minutes	97.5%
1% tincture of iodine	2 minutes	94.5%
70% alcohol	2 minutes	88.0%
1-1,000 tincture Zephiran (After thorough rinse to remove soap)	2 minutes	85.0%
1-1,000 tincture Zephiran (soap suds rinsed)	2 minutes	80.0%
50% alcohol - 10% acetone	2 minutes	70.0%
1-2,000 tincture of Metaphen	2 minutes	68.0%
1-1,000 tincture of Mercresin	2 minutes	60.0%
1-50 alcohol-acetone-aqueous Mercurochrome	2 minutes	45.0%
1-1,000 aqueous Zephiran (after thorough rinse to remove soap)	2 minutes	40.0%
1-1,000 tincture mercuric chloride	2 minutes	30.0%
1-1,000 tincture of Merthiolate	2 minutes	25.0%
1-1,000 aqueous Zephiran (soap suds rinsed)	2 minutes	0.0%

* Approximate within the limits of accuracy of the test method.[38]

in the order of their effectiveness: 1-2,000 Metaphen; 1-1,000 Mercresin; 50 percent alcohol—10 percent acetone alone; 1-1,000 mercuric chloride; and 1-1,000 Merthiolate.[38] None of these mercurials is sufficiently effective for the purpose to be recommended for preoperative use, although the antiseptic activity of the alcohol-acetone vehicle increased the activity of the mercurials to some extent. Since the tinctures of iodine, Zephiran, and certain mercurials gave degerming by this special "Degerming" test, the comparative reductions of skin bacteria may be compared on a suitable basis. Results of such tests are summarized in the table on page 555.

While these results do not necessarily reflect relative clinical effectiveness, they do represent the skin degerming properties of these antiseptics by an accurate method of comparison. Also it is quite likely that the margin of safety inherent in some of these germicidal solutions is such that there is actual overlapping in clinical effectiveness. Since there is no real basis for comparing percentage bacterial reduction by this method of test and clinical effectiveness in preventing infections from the skin at operation, the final criterion must, of course, be based on clinical experience in pre-operative use. However, it is quite evident from the above comparative data that alcoholic solutions of iodine and Zephiran are the most effective in reducing the numbers of skin bacteria and therefore are recommended for the purpose. As confirmation of this reduction, alcoholic solutions of iodine and Zephiran have been proved by extensive clinical experience to be effective skin antispetics for preoperative use.

It is apparent that the value of antiseptics used in hospitals must be, and in fact are, based on extensive research by a variety of suitable and acceptable test procedures. These tests follow a definite pattern, as has been illustrated here, first by laboratory and practical tests, which are then followed by clinical trials. Routine clinical application follows after such antiseptics have been proved efficient and effective by these three groups of tests. Antiseptics in the hospital pharmacy may therefore be used with confidence because of the extensive research supporting their effectiveness for use in hospital practice. That is the purpose of this brief survey of the subject.

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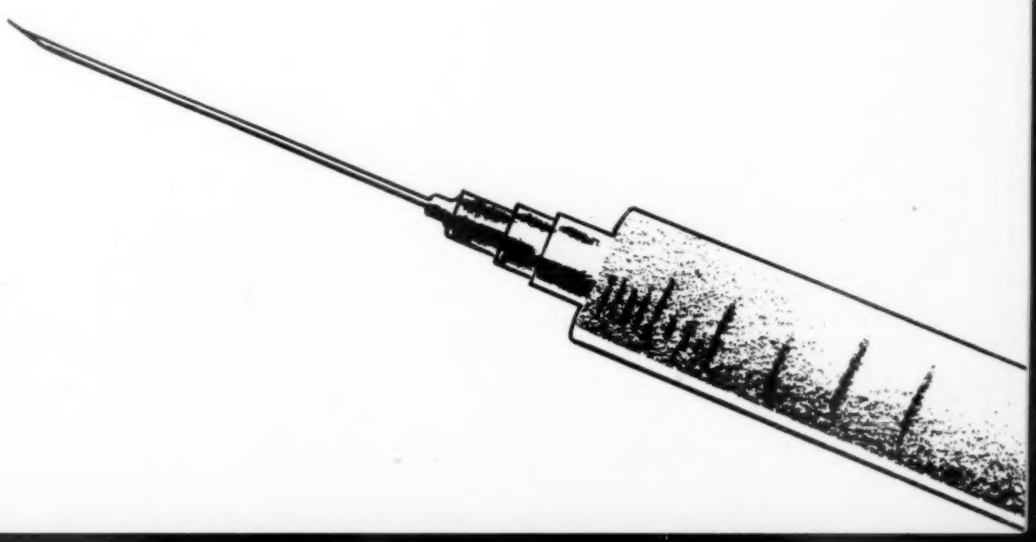
ANTIBIOTICS TODAY

A summary of recent developments in antibiotics reported at the recent symposium on antibiotics held in Washington, D. C.

THE FOURTH ANNUAL SYMPOSIUM on Antibiotics, sponsored by the Food and Drug Administration in collaboration with the journals *Antibiotics and Chemotherapy* and *Antibiotic Medicine and Clinical Therapy,* was held in Washington, D. C., October 17, 18, and 19. Recent discoveries and advances in the field of antibiotics were reported by leading scientists from the United States and abroad. A total of 156 papers were presented.

Several new antibiotics were described including oleandomycin, ristocetin, nucleocidin, hygromycin, alazopeptin, vancomycin, amphotericin, ascosin, and xanthocillin. Some of these antibiotics have been found effective against organisms resistant to the older antibiotic agents. Several papers on combined antibiotic therapy were presented. Chairman of the Symposium was Dr. Henry Welch, Director of the Division of Antibiotics, Bureau of Biological and Physical Sciences, Food and Drug Administration.

Because hospital pharmacists are closely associated with medical practitioners, an attempt is made here to present a brief account of the subjects covered. This résumé is based on information released by the Food and Drug Administration.



ALAZOPEPTIN is one of seven antibiotics produced by a hitherto undescribed species of *Streptomyces*, Lederle strain AA223. Alazopeptin has been isolated in crystalline form and found to be active against Sarcoma 180 in mice. Data suggests the empirical formula $C_{19}H_{21}O_6N_7$. Chemical and microbiological studies indicate that the molecule is composed of one mole of alpha-alanine and two moles of 6-diazo-5-oxo-L-norleucine (DON)[1].

AMPHOTERICIN B is an antifungal antibiotic derived from an unidentified species of *Streptomyces*. It has been found to inhibit the growth *in vitro* of various pathogenic and nonpathogenic fungi including *Candida albicans*. *In vivo* studies have shown that amphotericin B administered orally favorably influences experimental infections of candidiasis in mice. These findings suggest that this antibiotic might be useful in controlling the yeast flora of the gastrointestinal tract in man[2]. Amphotericin B offers considerable promise in adding significantly to the antifungal armamentarium in disseminated mycoses. It has been used successfully in experimental histoplasmosis and cryptococcosis. *In vitro* tests reveal a marked fungistatic effect against *H. capsulatum* and against *C. neoformans*[3].

Kozinn and associates reported on the use of amphotericin B in the treatment of cutaneous candidiasis in infancy and childhood. Twenty-five newborn infants and young children with cutaneous candidiasis in the diaper area were treated with Mycostatin locally, whereas 15 similar patients with a like skin eruption were treated with amphotericin B ointment. Eighty-four percent of the patients were cured with Mycostatin, and 80 percent with amphotericin. Only five to six days were required for cure when the lesions were recent and there was no pre-existing skin disease, whereas 17 to 18 days were required when the lesions were of long standing or superimposed on a dermatitis of other origin[4]. In another paper chemical studies on amphotericin B were reported and an empirical formula was proposed.[5]

ASCOSIN is an antibiotic which has been used in the treatment of 102 cases of scalp ringworm. The antibiotic was used in the form of an ointment in petrolatum. The lesions treated were those due to *M. audouini* and *M. lanosum*. After six to 27 weeks of treatment, there was cure or definite improvement in over 60 percent of the cases. The cumulative cure rate, after 12 weeks or more of treatment, was 50 percent. It is suggested that the addition of adjuvants such as keratolytics and hyperemics, plus epilation and massage, may be expected to further increase the rate of cure[6].

CHLORAMPHENICOL was studied over a five year period with respect to side effects and toxic reactions. Two thousand one hundred and eighty-two patients received chloramphenicol in therapeutic doses during this period of study. Of this group, 632 were selected for critical evaluation. The group comprised patients in the following categories: pertussis, 275; meningitis, 245; specifically diagnosed dysentery, 13; and typhoid fever, 99. Patients ranged in age from seven days to 86 years. They received a mean daily dose of 94.6 mg./Kg./day for an average of 16.5 days. Vitamin B complex and vitamin C were administered concomitantly with chloramphenicol. In this five year review and follow-up of patients, there were no changes in blood components beyond those usually observed in the disease entities treated[7].

In another study of the protracted intramuscular use of chloramphenicol in the treatment of tuberculosis, one gram of chloramphenicol was given daily for five days a week along with 4 mg. per kilogram of isoniazid. Blood studies were made every two weeks and pre-treatment and post-treatment bone marrow studies were made. No evidence of hemo-toxicity was observed. The antituberculous effect of the drug was not clinically impressive. However, due to the wide antibacterial spectrum of the drug, it was found useful in the treatment of lung abscess, non-tuberculous empyema, and suppurative pneumonitis[8].

A result of the third study indicates that chloramphenicol, similar to aminopyrine, may potentiate the effects of Myleran, a bone marrow depressant[9].

CYCLOSERINE (Seromycin, Lilly) tartrate has been given to ten tuberculous patients in doses of 250 mg. every 12 hours for four months. Toxic effects requiring cessation of the drug or a reduction of dosage occurred in two patients before the 12th day of study. No toxicity was observed after the first two weeks. Blood level studies showed 13 to 53 mg. of cycloserine, as the base, three hours after the last dose. Clinical effectiveness of the cycloserine tartrate was evidenced by bacteriologic and clinical improvement of the patients treated[10].

In another study a group of 29 patients with pulmonary tuberculosis was studied for from three to seven months under combined therapeutic regimen of 0.5 Gm. cycloserine in two divided doses and isoniazid in a dosage of 4 mg. per kilogram of body weight. All but three patients were original treatment cases. Sixty-five percent were far advanced; 35 percent moderately advanced. All had positive sputa and all had cavities. Five patients left against medical advice after two to three months. Four were negative, two on culture. Of the remaining 24 patients, 14 were negative on smear and concentrate; ten were positive. At the time of the report half of the negatives were substantiated by three month cultures. Among the "positives" are three patients thoroughly resistant to well-known agents and persistently sputum-positive for three to five years. Two of these relapsed after persistent negativity for three months after institution of therapy. Resistance studies on these are pending. All cases treated with the combination showed some improvement. There was no deterioration. All x-rays showed some improvement[11].

ERYTHROMYCIN was studied for its effectiveness against respiratory infections. It was found to possess not only a high predictability of effectiveness for the treatment of commonly encountered respiratory infections, but the antibiotic is safe for chronic administration[12]. Erythromycin lactobionate, administered as an aerosol, was found to be effective in controlling chronic bronchial infections[13]. In studies on the concentration of erythromycin in the bronchial tree after oral, intravenous, and aerosol administration it was found that the drug is present early in high concentration in the bronchial tree, depending upon the method of administration. Adequate levels in the bronchial tree are maintained for several hours[14]. Mouratoff and associates studied the effectiveness of erythromycin for the treatment of chronic genito-urinary infections and found that it is an effective and safe antibiotic for the treatment of chronic genito-urinary infections[15]. Studies on the use of oral erythromycin in the treatment of acne vulgaris and other dermatoses were presented. In this paper it was noted that

there was no correlation between organism sensitivity and clinical results. The paper tabulates and evaluates the results obtained in various skin disorders treated with oral erythromycin[16]. A paper by Tidwell and Lewis concludes that erythromycin appears to be an adequate substitute for penicillin as a prophylactic antibiotic agent in the suppression of beta-hemolytic streptococcal infections[17]. A study by Clapper and associates indicates that erythromycin is effective in the treatment of respiratory and other infections in which sensitive organisms were the cause. There was no evidence of establishment of resistant staphylococci, yeasts, or enteric bacilli in any of the throat and sputum cultures[18].

HYGROMYCIN is a new antibiotic isolated from a strain of *Streptomyces hygroscopicus*. The antibiotic is effective against a variety of gram-positive and gram-negative bacteria. It is also active against several species of parasitic organisms including *Endamoeba histolytica in vitro* and *in vivo*, *Borrelia novyi in vivo*, *Leptospira pomona in vitro*, and oxyurids in mice. The effect of hygromycin is very favorable when compared with other broad-spectrum antibiotics. The antibiotic appears to be ineffective against Toxoplasma, *Trichomonas vaginalis*, *Trypanosoma equiperdum*, and *T. gambiense*[19].

NOVOBIOCIN (Albamycin, Upjohn; Cathomycin, Merck Sharp & Dohme) is an acidic, crystalline antibiotic obtained from *Streptomyces spheroides* and from *Streptomyces niveus*. It is a white crystalline powder with a yellow tint and has an approximate molecular formula of $C_{31}H_{42}N_2O_{11}$. It is a dibasic acid and is more soluble in alkaline than in acid solutions; the latter, however, are more stable. Novobiocin has a low order of toxicity and is effective against a selected group of gram-positive and gram-negative organisms, including *M. pyogenes* var. *aureus* and *B. proteus*. Corbin and Prigot report that whether the antibiotic is administered orally, intramuscularly, or intravenously it appears in plasma and urine at levels well above the *in vitro* inhibitory concentrations. The antibiotic was not detected in spinal fluid specimens in this study[20].

Trafton and Lind reported on the use of novobiocin in the treatment of urinary tract infections. Many of these cases had been previously treated with one or more antibiotics with little or no improvement. The organisms encountered included *Proteus sp.*, *Micrococcus aureus*, enterococcus, *E. coli*, and *Aerobacter aerogenes*. Tolerance to novobiocin was good. The clinical response ranged from improvement to clinical cure except in three cases involving *Micrococcus aureus*, *E. coli*, and *Proteus vulgaris* where no improvement was encountered[21].

Lepper and associates reported the use of novobiocin and spiramycin in combination. In studying the effects of novobiocin and spiramycin in combination against resistant strains of hospital staphylococci, it was found that the development of the spiramycin-resistant pattern was considerably slower than when this drug was used alone in a previous comparable study. The novobiocin resistance developed less completely than was true for previously studied drugs[22].

Shidlovsky and associates used novobiocin alone and in combination with neomycin in a screening program of antibiotics for intestinal antisepsis. Novobiocin was chosen because of its activity against such micro-organisms as *Micrococci*, *Streptococci*, and *Proteus*. It appears that novobiocin would prove more effective when combined with a second chemotherapeutic agent active against various gram-negative flora which are not sensitive to novobiocin. Of the dosage schedules employed in this preliminary screening, the combination of 500 mg. of novobiocin with 500 mg. of neomycin administered orally four times a day resulted in the greatest reduction in the number of both gram-positive and gram-negative bacteria in a gram of wet stool. During the course of these experiments no toxic manifestations or side reactions were observed or reported by any of the patients[23].

High and Huang show that a variety of staphylococcal infections in infants and children have been satisfactorily treated with novobiocin. The types of infections included impetigo neonatorum, pyodermia, cellulitis, nasopharyngeal infections and carrier states, septicemia, and pulmonary infections. No significant untoward reactions were noted and no drug reactions were observed. The preparations of novobiocin included material for parenteral use, capsules, a pediatric suspension, and pediatric drops[24].

Novobiocin was used by Garson and McLeod in a study to determine its effect on *Treponema pallidum in vivo*. Data accumulated indicates that novobiocin has a definite measurable antitreponemal effect on rabbits under the conditions of this experiment[25].

Novobiocin was used by Findlay and Johnson in the treatment of postsurgical diarrheas in 11 patients. The dosage was 250 mg. orally four times a day for three days, except in one case of fulminating enterocolitis. In the latter case the patient made an excellent response to combined intravenous and oral therapy for four days, followed by two days of oral treatment. With one exception, a striking decrease in the number of staphylococci was noted on the second day of treatment. Staphylococci were eliminated from the stools of six of the eleven patients within three days. In the remaining five cases, the number became insignificant. One patient developed urticaria within a few days after treatment was stopped. This responded readily to treatment. The authors found that novobiocin effectively reduced or cleared multi-antibiotic-resistant staphylococci from the intestinal tract[26].

Cook and associates reported clinical experiences with novobiocin. Nineteen patients with acute pneumococcal or staphylococcal infections were given two grams of novobiocin orally daily. Pneumococcal infections responded favorably. One patient with staphylococcal pneumonia died but his blood cultures were sterilized. The other three with pneumonia cleared by lysis. All cases of furunculosis improved although recurrences developed in two of the three upon cessation of therapy. A patient with endocarditis recovered. In this series, nine instances of untoward side reactions were observed. Five patients developed mild gastrointestinal distress. Four developed generalized morbilliform rashes serious enough to warrant cessation of therapy[27].

Rivera and colleagues compared the action of novobiocin and seven other antibiotics on *M. pyogenes* isolated from infections in burned patients. The other antibiotics were penicillin, oxytetracycline, chlortetracycline, polymyxin, chloramphenicol, erythromycin, and bacitracin. In a series of patients from whom 378 cultures were made, 214 *M. pyogenes* strains were isolated. Novobiocin was more effective as compared with the other antibiotics. In another series of patients, bacitracin was more effective (99 percent) as compared with novobiocin (65 percent). In a third series of

patients the action of three antibiotics was studied. Novobiocin was 100 percent effective against *M. pyogenes* as compared with erythromycin which was 65.6 percent, and with penicillin which was 7.5 percent effective[28].

David and associates reported on the use of novobiocin preparations in hospital practice. Some of the patients were given an initial intramuscular injection of 250 mg. of novobiocin dissolved in 2 ml. of diluent. These patients were later transferred to oral therapy. In other patients only oral therapy was used. Cultures done on 25 of 35 patients showed the presence of hemolytic *Staphylococcus aureus* in 21, *E. Coli* in 4, *Pseudomonas aeruginosa* in 3, *Aerobacter aerogenes* in 2, Proteus in 2, and Gamma streptococcus in 1. In 17 cases these organisms were found sensitive to novobiocin, and only to this antibiotic in three staphylococci and one *E. coli* infections. Untoward reactions included four patients with rashes, seven who showed an eosinophilia from 5 to 17 percent, four with nausea and vomiting, one with drug fever, and one ambulatory patient had vertigo from time to time during the 47 days she took novobiocin. No evidence of neutropaenia or jaundice was found and repeated serum bilirubins done on six patients were normal. Response to novobiocin therapy was considered as excellent in 10 patients, good in 16, fair in 6, and none in 3. The authors also used the syrup of novobiocin in a series of eleven children in whom nine were in a group of 13 infants treated for epidemic staphylococcus pyoderma affecting the skin and scalp. The rather large dose of 125 mg. was given four times a day, and usually in conjunction with triple sulfonamide therapy, for periods of from 13 to 16 days. Novobiocin was well tolerated and more effective than previously tried antibiotics[29].

NUCLEOCIDIN is a new antibiotic produced by an unidentified streptomyces species, tentatively designated as Lederle strain T3018, which was isolated from a soil sample obtained from Dienpur, India. Analyses suggest the empirical formula $C_{11}H_{16}N_6O_8S$. Nucleocidin exhibits *in vitro* activity against a variety of gram-positive, gram-negative, and acid-fast bacteria. No protection was observed when nucleocidin was administered parenterally to mice infected with a sensitive strain of *Streptococcus pyogenes* C203. When administered parenterally to mice infected with *Trypanosoma equiperdum,* nucleocidin exhibited curative effects at single dosage levels as low as 0.02 mg. per Kg[30].

Another study showed that nucleocidin is highly effective *in vivo* against *Trypanosoma equiperdum.* Curative effects with pure crystalline material were obtained with 0.02 to 0.05 mg. per Kg. parenterally and 0.6 mg. per Kg. orally, when given to mice in single doses within a few hours after inoculation with trypanosomes. Nucleocidin is approximately 40 times more active than Antrycide or Naphuride sodium and 4,000 times more active than Stylomycin puromycin against *T. equiperdum* in mice[31].

OLEANDOMYCIN (Matromycin, Pfizer) is a basic antibiotic produced by a strain of *Streptomyces antibioticus.* It is active principally against certain gram-positive and a few gram-negative organisms and has also demonstrated *in vitro* activity against some of the larger viruses and some *Rickettsiae.* Upon oral administration of oleandomycin to humans, serum levels and urine levels were demonstrated which exceeded the *in vitro* sensitivity of certain gram-positive and gram-negative organisms to the antibiotic. In animals, the orally administered antibiotic was well tolerated and there was no evidence of toxicity in those receiving 300 mg. per kilogram of weight five days a week for periods of from six to nine weeks[32].

Marmell and Prigot presented a report on the use of oleandomycin in gonorrhea in the male and concluded that in adequate doses the antibiotic is effective in the treatment of this disease[33]. A report was presented by LaCaille and Prigot on the combinations of oleandomycin with oxytetracycline and tetracycline in the treatment of soft tissue infections. Results indicate that these combinations of antibiotics are clinically effective and although side reactions occur, they are minimal. The synergistic action of these combinations, as related to their therapeutic effectiveness in this study, has not been proven[34]. Another paper reported on the effect of oleandomycin alone and in combination with neomycin on intestinal microflora. In all groups where oleandomycin was used alone, the gram-positive flora was reduced. When oleandomycin was combined with neomycin, both the gram-positive and gram-negative organisms were reduced numerically per gram of wet stool[35].

Marmell and Prigot reported on the use of a combination of oxytetracycline and oleandomycin, in the proportion of two to one, in the treatment of lymphogranuloma venereum and acute gonococcal urethritis in the male. On a daily dose of one gram of the combination, the patients with lymphogranuloma venereum were cured in 15, 18 and 20 days, respectively, with complete healing of the lesions. Ten of the 30 patients with gonorrhea received a total dosage of 1.5 Gm. of the combination in divided doses. Nine of these were cured and the one failure is attributed to the excess intake of alcohol by the patient while under treatment. Of the remaining 20 patients, who received one gram of the combination, 15 were cured[36]. Carter reported on a series of clinical trials with oleandomycin in combination with Terramycin and also in combination with tetracycline. He concluded that this combination is an excellent addition to the therapeutic armamentarium of the clinician[37].

Loughlin and Mullin reported on the use of oleandomycin combined with either oxytetracycline or tetracycline in the therapy of tropical infections. The combinations used were oxytetracycline 67 percent and oleandomycin 33 percent, or tetracycline 67 percent and oleandomycin 33 percent (Sigmamycin). These combinations were used in a variety of infectious diseases such as amebiasis, yaws, lymphopathia venerea, and tropical ulcer. More than 130 cases were treated. It was found that these diseases generally have responded more rapidly, have required smaller doses and less extended periods of therapy than when treated with the tetracycline alone. The clinical results obtained with these tetracycline-oleandomycin combinations in the treatment of tropical infections, when compared with those obtained with the tetracyclines given singly, not only apparently confirmed the results of the biologic studies but also seem to indicate that these antibiotic combinations possess an even greater range of antimicrobial synergistic activity extending to infections caused by certain protozoas, viruses, treponemas, and spirochoetes[38].

PA-105 is a new antibiotic active against gram-positive organisms. It has recently been employed in combination with tetracycline (67 percent tetracycline and 33 percent PA-105). The combination was used in 50 hospital cases, including pyodermas, osteomyelitis, genito-urinary tract infections, acute cholecystitis, skin

ulcers, and oral sepsis. Staphylococci were present in most infections. Sixty percent of the cases had been treated previously with other antibiotics without therapeutic response. In the present study, combined therapy with PA-105 and tetracycline was administered in one capsule (300 mg.) four times daily for a period ranging from 7 to 21 days. Favorable therapeutic response was obtained in 96 percent of the cases. The only side effect was an occasional soft stool[39].

PA 132 is a new broad-spectrum antibiotic which is active against three widely separated classifications of microorganisms. The *in vitro* spectrum studies indicate a good activity against both gram-positive and gram-negative bacteria, good activity against a wide variety of pathogenic and saprophytic fungi, and good activity against the protozoa *Trichomonas vaginalis* and *Endamoeba histolytica*[40]. However, since the antibiotic appears to be highly toxic, as shown by *in vivo* studies in mice, it is believed that the most promising use for this new antibiotic will be against the plant pathogenic fungi such as *Alternaria solani* and *Pythium debaryanum*[41].

PENICILLIN V, or phenoxymethyl penicillin, was the subject of five reports. Brown and associates reported observations on the absorption, excretion, and clinical effects of phenoxymethyl penicillin. Blood level estimations of phenoxymethyl penicillin in normal subjects after varying dosages indicate that a peak concentration is reached at about one hour when the dose is taken fasting, and that the appearance of the peak is delayed until two hours when taken after a meal. A therapeutic level can be demonstrated in the blood for at least four hours after a dose of 120 mg. or more. Urinary excretion experiments show that an average of 27 percent of the dose administered is excreted in the urine within six hours and that most of this (24 percent) appears within three hours. The authors presented a composite list of clinical results in the treatment of various infections. The large percentage of satisfactory results obtained compares favorably with those achieved by penicillin therapy administered by the parenteral route[42].

Cox and associates reported on the use of large doses of oral penicillin V in the treatment of serious infections. Administration of 1200 mg. doses of oral penicillin V results in serum concentrations of 1.7 to 2.8 times greater than when oral penicillin G is given. When multiple 1200 mg. doses of oral penicillin V were administered for prolonged periods, it was found that a significant degree of penicillinemia was maintained and higher average serum concentrations were achieved. Serum accumulation of oral penicillin V occurred in fifty percent of subjects who received 1200 mg. every four hours for 96 hours. The effects of the renal blocking agent probenecid, in a dose of two grams daily, on serum concentrations were studied and it was noted that penicillin V plus probenecid results in serum concentrations 3.2 to 3.8 times greater than the combination of penicillin G and probenecid. The use of probenecid apparently produced an increased capillary fragility in some patients. The authors reported the successful treatment of 13 of 14 cases of bacterial endocarditis with the high oral dose regimen of penicillin V[43].

Wehrle and associates reported on the use of penicillin V in the treatment of scarlet fever and acute streptococcal pharyngitis. Sixteen children with scarlet fever, and seven adults and children with confirmed streptococcal pharyngitis were studied. Therapy consisted of penicillin V, 200,000 units administered orally every eight hours for ten days. Eighty percent of the patients were afebrile within 24 hours, and only two remained above 100 degrees longer than 72 hours. Cultures for streptococci were uniformly negative after the fifth day, and fell promptly from 67 percent positive initially to 23 percent positive within twenty-four hours after institution of therapy[44].

Finke reported on the use of penicillin V in the prophylaxis of disabling respiratory infections in susceptible children. He studied 31 school children with chronic bronchitis or infectious asthma. These children received prophylactic treatment during February and March with penicillin V as the chief antibiotic. The average daily dose was one gram, which was increased if significant respiratory symptoms occurred. For more prompt suppression of the devoloping infection, eight children received sulfonamides and six received tetracycline in addition to penicillin V for from three to six days. During the two month period the penicillin V-protected children missed an average of seven percent of possible school days while in a series of 68 children with chronic bronchitis or infectious asthma not protected with antibiotics, the group missed an average of 13 percent of possible school days[45].

McWhorter and associates reported on the treatment of moderate and severe lobar pneumonia with oral penicillin V. Results of this study indicate that oral penicillin V is effective in the treatment of patients with lobar pneumonia of moderate to severe degrees of illness. The dosages used were 375 mg. every four hours, 300 mg. every four hours, or 300 mg. every six hours. No clinical differences could be detected in the responses to the three dosage schedules. Ninety-three percent of the patients made satisfactory responses[46].

Smith and co-workers studied the binding of penicillins G and V by human plasma. Using the dialytic technic, they found that the degree of binding of penicillin V by human plasma is considerably higher than that of penicillin G. They pointed out that this finding may have important therapeutic implications. In most publications comparing penicillins V and G, attention has been directed almost entirely to the total concentrations in plasma or serum without consideration of the relative concentrations of free penicillin[47].

BENZATHINE PENICILLIN G in the control of gonorrhea was the subject of a report by Hookings. He noted a significant reduction in the cases of gonorrhea after 1.2 million units of benzathine penicillin G were added to the treatment regimen[48]. Tidwell reported on the use of benzathine penicillin in rheumatic fever. Over a two-year period, up to 1,400 people in the state of Washington were on daily benzathine penicillin prophylaxis in a rheumatic fever control program. There were only two instances of reported drug reaction and no reported recurrences of rheumatic fever in those patients who took the medication as prescribed. Results of the prophylactic use of benzathine penicillin in other groups were also described[49].

NEW PENICILLIN SALTS. Four studies were reported on new salts of penicillin. Hobby and co-workers reported a crystalline salt formed by the chemical combination of penicillin and oleandomycin. These two antibiotics are active principally against gram-positive micro-organisms. Their study also reported on the action of this new crystalline salt when combined with potassium or procaine penicillin G[50]. Muckter and associates reported a new antihistamine salt of penicillin. They reported that the antihistamine, 1-p-chlorbenzyl-2-pyrro-

lidyl-methylbenzimidazol, forms an insoluble salt with penicillin. This new procaine-free depot penicillin is soluble to the extent of 0.025 to 0.03 percent in water. The acute and chronic toxicity of this antihistamine penicillin by subcutaneous application in the mouse is less than that of procaine penicillin. By interperitoneal injection the acute toxicity is the same as procaine penicillin. In combination preparations, containing 100,000 units sodium penicillin G and 300,000 units of antihistamine penicillin, or 200,000 units of sodium penicillin G and 800,000 units of antihistamine penicillin, therapeutic effective blood levels were found for 36 to 48 hours or five to seven days, respectively, in single intramuscular injections in humans. When compared to procaine penicillin, the new antihistamine depot penicillin is the same in its antibacterial activity; however, toxicologically and with respect to the depot effect, it is superior. Primarily it shows clinically a small allergenic potential since many of the so-called penicillin allergies can be explained as procaine hypersensitivities[51].

Another report was presented on the antimicrobial activity of serum of humans after the oral administration of the oleandomycin salt of penicillin G, with and without added potassium penicillin G. Seven case reports were presented to indicate the clinical effectiveness of these preparations in the treatment of a variety of infections[52].

Muckter and associates reported on the choline ester of penicillin, especially as the hydrobromide salt. Pharmacologically, a short-lived curare-like effect was demonstrated which could not be relieved by the common antidotes, such as physostigmine or atropine, while in the case of overdose it could only be cured by artificial respiration. The penicillin-choline ester has been shown in animal experiments and in man to have a selective affinity for the liver-gall system, with gall bladder levels of active penicillin 10 to 20 times that obtained from sodium penicillin G. It was concluded that the choline ester of penicillin may be, under careful indications and application technics, a valuable therapeutic adjunct to the treatment of infectious processes of the liver-gall system. Its use in combination with streptomycin was suggested[53].

Penicillin and Aerosol O.T. in combination were used in the treatment of chronic osteomyelitis by topical application. Instillation of 2 to 3 ml. of a solution of 10,000 units of penicillin and Aerosol O.T. 1:1,000 was carried out every four hours for ten days. Supplemental intramuscular injections of 20,000 units of penicillin every three hours for the first four days as well as general supportive therapy were used in addition. The study comprises 95 cases of chronic pyogenic osteomyelitis. A total of 64.21 percent of patients had complete arrest of the disease for periods of from one to five years. Patients were hospitalized for an average period of two weeks and were ambulatory at the termination of treatment[54].

PENICILLIN RESISTANT SPIROCHETES. Ercoli and associates reported that they were able to obtain a strain of relapsing fever spirochetes (*B. novyi*) which requires five to ten times higher penicillin doses than the original for equivalent therapeutic action. Exposure of a freshly collected spirochetal blood suspension diluted with tryptose broth contained in glass test tubes to 40,000 roentgens of soft x-rays was one of the steps employed in the development of a penicillin resistant spirochete[55].

RISTOCETIN is a new antibiotic produced from the actinomycete *Nocardia lurida*. It is active against gram-positive bacteria and mycobacteria. Ristocetin is relatively nontoxic, has marked bactericidal properties, and resistance to it is not readily acquired. The activity is little influenced by blood and serum[56]. The *p*H does not significantly alter the activity. The antibiotic is bactericidal for *Mycobacterium tuberculosis in vitro*[57].

Ristocetin is not absorbed by the oral route and currently is used primarily by the intravenous route where high concentrations are obtained in the blood. Striking results were obtained in patients with enterococcal infection and good results obtained against enterococcal bacteremia. Patients received ristocetin intravenously in doses as large as four grams per day. This dosage was well-tolerated without side effects[58].

SULFA METHOXYPYRIDAZINE (Kynex) is a new antibacterial sulfanilamide with activity equal to sulfadiazine and with very favorable pharmacological properties. The drug is rapidly absorbed from the gastrointestinal tract with maximal blood levels reached after 2 to 3 hours. Thereafter the concentration falls very slowly. The urinary excretion is very slow and the degree of acetylation of the drug is small. During continued treatment (1 Gm. every 12 hours) the lowest blood concentration during the day was about 20 mg. percent. No sulfa crystals were detected in the urine. In 30 cases of both acute and chronic pyelonephritis good results (sterile urine after treatment) were obtained in 50 percent of the cases. Except one case with drug fever and one with nausea, no other side reactions were observed[59].

STREPTOMYCIN was the subject of five papers presented. Experimental evidence supports the hypothesis that streptomycin acts by preventing an increase in the differential rate of synthesis of enzyme and that this effect is directly related to the inhibition by streptomycin of the multiplication of susceptible organisms. The site at which streptomycin reacts in the cell appears to be a nucleic acid component[60]. Four papers concerned the toxicity of streptomycin, especially the influence of the pantothenate salts on toxicity. German workers believe that high streptomycin doses cause an acute defiency of ionized calcium without reducing the total blood calcium. The central nervous system reacts first with a narcosis-like state, followed by death through paralysis of the respiratory system. Pantothenic acid does not form a simple salt with streptomycin but probably a complex, saturating the co-valences of streptomycin so that in the body streptomycin pantothenate ties up less calcium than streptomycin. In acute experiments this is the reason that streptomycin pantothenate is less toxic. They present the hypothesis that pantothenic acid forms a protective factor for organs which are phylogenetically derived from the ectoderm[61]. Osterberg and associates found no differences between the streptomycin salts when tests for vestibular damage using postrotatory nystagmus in mice or equilibrium studies on the cats were made. However, in studies on hearing loss in rats with dihydrostreptomycin, the pantothenates were effective in preventing the loss of auditory acuity which was observed after prolonged administration of the sulfate[62]. Child and co-workers found that streptomycin pantothenate is slightly more toxic than streptomycin sulfate when injected subcutaneously in mice, but the pantothenate of dihydrostrep-

tomycin is less toxic than the corresponding sulfate[63]. Hawkins and associates were unable to confirm the claim by German workers that pantothenic acid reduces the ototoxicity of either streptomycin or dihydrostreptomycin[64].

SYNNEMATIN B is a new type of penicillin with the D-4-amino-4-carboxy-n-butyl group as the side chain. Its sodium salt is estimated to have a molecular weight of 381 and a potency of about 700 units per mg[65]. It is identical to another antibiotic, Cephalasporin N[66]. After oral administration, Synnematin is poorly absorbed primarily because of its chemical nature. However, after intramuscular administration the antibiotic is well absorbed and significant blood and urine levels are obtained[67]. Synnematin B, when compared *in vivo* by mouse protection tests with chloramphenicol, chlortetracycline, polymyxin B, and streptomycin, was found to be the most effective antibiotic against the organisms *P. mirabilis* and *S. typhimurium*. In addition, it was effective against *E. coli* and *P. vulgaris*[68]. With some differences, the antibacterial spectrum of Synnematin B is similar to that of penicillin G; however, the two antibiotics appear to exert their antibacterial effect through different mechanisms[69]. Another study reported on attempts to evaluate the antimicrobial activity of Synnematin B, and to compare its activity, particularly against strains of the Salmonella species, with that of chloramphenicol, oxytetracycline, and polymyxin B[70].

TETRACYCLINE was reported effective in the treatment of two cases of leptospirosis. Therapy was initiated on the sixth day of illness. One patient received one gram daily by mouth while the second patient was given 0.1 Gm. intramuscularly every six hours for five days followed by one gram of tetracycline by mouth. On this regimen the fever receded gradually, jaundice improved, there were no new hemorrhagic effusions and those present diminished[71]. Three studies were reported on the effect of tetracycline plus nystatin on the intestinal flora of man. The addition of nystatin does appear to be effective in reducing the number of fungi and to prevent their overgrowth in the gastrointestinal tract. This is particularly true with *Candida* organisms [72,73,74].

In the treatment of purulent meningitis a dosage of 75 mg. of tetracycline per kilogram of body weight produces reliable therapeutic blood and cerebrospinal fluid levels. The tetracycline was administered intramuscularly[75]. Other papers reported on the use of tetracycline in the treatment of acute infections[76], its evaluation in bronchiectasis and chronic bronchitis[77], and in the treatment of surgical infections[78].

VANCOMYCIN (Vancosin, Lilly) is an antibiotic obtained from a species of *Streptomyces orientalis*. It is highly active against gram-positive cocci. Several studies on vancomycin were reported. Vancomycin has a low order of toxicity, LD_{50} by intravenous injection in mice is about 400 mg. per Kg. Chronic toxicity studies in rats and in dogs and monkeys showed no hematopoietic or visceral damage after six months of therapy[79]. Following multiple intravenous doses of 0.5 Gm. every six hours, average values of 8.5 micrograms per milliliter are found in the serum. Vancomycin diffuses through pleural, pericardial, peritoneal, and synovial membranes. It is excreted in the bile, urine, and feces in therapeutic amounts but does not cross the uninflamed meningeal barrier[80].

Serum concentrations following the intravenous administration of 0.5 to 2.0 Gm. are quite high, and vancomycin seems to persist in the blood stream for a longer time than any other antibiotic. Thrombosis of veins has occurred in a few instances and tissue irritation occurs when the antibiotic leaks out of the vein. Low-grade fever due probably to the antibiotic has occurred in several patients. Three others developed high fever. Vancomycin appears to be a very promising antibiotic for the treatment of staphylococcal infections[81].

Oral administration of 0.5 Gm. of vancomycin does not produce assayable blood levels. However, therapeutic concentrations are obtained in the urine, indicating that a small proportion of the antibiotic is absorbed from the intestinal tract[82].

Following intramuscular injection vancomycin passes through the placenta from the maternal blood to the fetal blood and amniotic fluid of rabbits, and is present in the milk of lactating cats[83].

XANTHOCILLIN is a crystalline, stable, yellow antibiotic. It was isolated in 1948 from a mycellium of a *Penicillium notatum* stock by Rothe. The new antibiotic shows a broad antibacterial spectrum against gram-positive and gram-negative organisms, including *B. proteus* and *Ps. aerogenes*, also against the tubercle bacillus, fungi, and molds. Xanthocillin resembles tyrothricin as far as tolerance and slow resorption are concerned. In fact, tyrothricin intensifies the activity of xanthocillin. The combination is also called TX and is marketed in Germany under the trade name Tyrocid X. Xanthocillin either alone or in combination with tyrothricin is used in local therapy. The bacterial spectrum is said to be complete and the tolerance good. No change of infection, such as the overgrowth of dermatophytes or candida, is observed in the treatment with xanthocillin. Xanthocillin is said to offer a routine local antibiotic therapy without risking the development of resistant strains and increasing the allergenic potential in patients[84].

ANTIBIOTIC COMBINATIONS. Several studies were reported on the use of different antibiotics in combination for the treatment of different disease conditions.

Seneca reported on the use of tetracycline, nystatin, and novobiocin in amebiasis. *In vitro* studies revealed that the minimum inhibitory concentration of novobiocin to cultures of *Endamoeba histolytica* was 1:2,400; nystatin 1:1,200; tetracycline 1:19,600; novobiocin plus nystatin 1:1,200; novobiocin plus tetracycline 1:76,800; nystatin plus tetracycline 1:76,800; and nystatin plus novobiocin plus tetracycline 1:102,400. Thirteen patients were treated with 250 mg. of tetracycline and 250,000 units of nystatin four times daily for ten days. Twenty-four cases were treated with novobiocin and tetracycline 250 mg. of each four times daily for ten days. Thirteen patients were treated with 250 mg. of tetracycline, 250 mg. of novobiocin, and 250,000 units of nystatin, four times daily for ten days. During the follow-up period, there was clinical improvement and the stools were negative for *E. histolytica*[85].

Elliott and Hall studied the synergistic action of 12 antibiotics against 30 strains of *Staphylococcus aureus*. The activity of 12 antibiotics singly and in pairs was measured against 30 strains of coagulase-positive, hemolytic *Staphylococcus aureus* recently isolated from patients. The antibiotics included penicillin, streptomycin, chlortetracycline, oxytetracycline, tetracycline, chloramphenicol, neomycin, bacitracin, erythromycin, cycloserine, vancomycin, and novobiocin. It was found that strains resistant to the bactericidal action of peni-

cillin usually were resistant to streptomycin and the tetracyclines. All the strains were sensitive to bacitracin, neomycin, chloramphenicol, cycloserine, novobiocin, and vancomycin. Only one strain was resistant to erythromycin. Penicillin, bacitracin, neomycin, erythromycin, streptomycin, and the tetracycline group all had marked bactericidal activity against many strains. Chloramphenicol, novobiocin, and cycloserine were largely bacteriostatic. Vancomycin was strongly bacteriostatic against all strains but its bactericidal activity was variable. Additive bacteriostatic activity was found with 32 of 66 antibiotic pairs. Synergism and antagonism of bacteriostasis were infrequent with any combination. Replica plating showed additive or synergistic bactericidal activity with 31 of 66 combinations and was especially frequent with the combination of chloramphenicol with bacitracin, erythromycin, vancomycin, or neomycin; bacitracin with erythromycin, cycloserine or vancomycin; erythromycin with cycloserine; neomycin with cycloserine or novobiocin; vancomycin with novobiocin, cycloserine, chlortetracycline, streptomycin, tetracycline, or oxytetracycline. Antagonism was uncommon with any combination including bacteriostatic with bactericidal antibiotics[86].

Meleney and Johnson reported on the use of oral bacitracin and neomycin to produce sterilization of the alimentary tract. Complete sterility was not obtained in every case by any of the methods used, either with the combination of bacitracin and neomycin or in a control series with neomycin alone. Sterility or marked reduction in the number of bacteria and of species was obtained in 90 percent of the gastric cases and in 70 percent of the bowel cases. The tablets with 10,000 units of bacitracin methylene disalicylate and 100 mg. of neomycin gave the highest percentage of sterile cultures[87].

Kayser and associates reported on the treatment of pneumonia with a combination of tetracycline and nystatin. Twenty-six cases of primary pneumonia were treated with the combination. The results and incidence of side effects were similar to those expected from treatment with tetracycline alone in similar cases. Therefore, this combination of antibiotics can be used effectively and safely when the indications arise[88].

Shidlovsky and Turell reported on the use of Soframycin (Roussel) in combination with nystatin as an intestinal antiseptic. An attempt was made to determine whether the combination of a broad-spectrum antibiotic such as Soframycin and the antimycotic drug, nystatin, would effectively reduce the various groups of microorganisms found in the intestines of man. Ten patients were employed in this study, two groups of five each. The first five patients received 500 mg. of Soframycin and 500,000 units of nystatin four times a day. The second group received 500 mg. of Soframycin, in addition to 1,000,000 units of nystatin four times in one day[89].

Spaulding and associates had previously reported that the triple combination of neomycin, polymyxin B, and nystatin is the most effective combination for intestinal antisepsis. Additional studies have demonstrated that almost as good results can be obtained if the polymyxin B is omitted and the daily dosage of nystatin reduced from three million to one million units. Furthermore undesirable side effects are minimal if a total dose schedule of 4.5 Gm. of neomycin and 1,125,000 units of nystatin are given over a period of 16 hours. Doubling these amounts and extending the medication period to 24 hours increases the toxic but not the antimicrobial effects[90].

Cohn and Longacre presented a comparison of various antibacterial agents in the preoperative sterilization of the colon. They have completed studies with the following agents: Sulfasuxidine, Sulfathalidine, chloramphenicol, novobiocin, chlorquinaldol, erythromycin, erythromycin-neomycin, chlorquinaldol-neomycin, oxytetracycline-neomycin, and Sulfathalidine-neomycin. Bacteriologic results, sensitivity studies, and significant side reactions were presented. The authors state that a number of these agents are not satisfactory for preoperative intestinal antisepsis and should be discarded[91].

STEROIDS AND ANTIBIOTICS. Lepper and Spies reported the clinical study of the use of cortisone, hydrocortisone, and corticotropin in the treatment of seriously ill patients with infections. The use of steroids produced no reduction in the total death rates or deaths in the first 24 hours of any of the serious bacterial infections. Serious bacterial complications such as pseudomonas and staphylococcal bacteremias were frequent among the 124 patients treated[92].

Shubin, in another study, reported the effects of steroids on patients with tuberculosis. In a series of 20 patients suffering with acute forms of tuberculosis, either miliary, meningitis, or pneumococcic, the simultaneous administration of Sterane with antituberculous drugs oft times proved life-saving. The author believes that the use of Sterane in conjunction with antituberculous chemotherapy is of tremendous value in acute tuberculous patients and that its use in chronic tuberculosis shows value and would be a means of converting many of these patients to a noncontagious disease[93].

BURNS AND ANTIBIOTICS. Two papers were presented on the local management of burns using antibiotics and other drugs. Garnes and Maynard reported a series of second and third degree burns treated with tetracycline-neomycin spray powder. In no case did gross infection of the burn wound occur and wound healing was not retarded. In the second degree burns, healing proceeded under the escar without complication. In the third degree burns, separation of slough was not delayed as compared with closed therapy and the "take" of skin grafts was not interfered with[94]. Shelby and Prigot also used tetracycline and a tetracycline-neomycin combination in the local management of infected wounds. The tetracycline was prepared as a powder spray and the tetracycline-neomycin in the form of a powder spray or a spray dressing. Enzymatic debridement with streptokinase-streptodornase and with activated whole raw pancreas was also used. The results indicate that in the management of open infected wounds using enzymatic debridement and spray application of antibiotics there is an increased expectancy of successful healing or satisfactory preparation of the area for resurfacing[95].

SENSITIVE AND RESISTANT ORGANISMS. Engley and Bass presented a study of the comparative antibiotic resistance of airborne micro-organisms isolated from hospital areas. Wide variation in the susceptibility or resistance patterns of organisms was observed in the microbial population from the air of different areas. The data indicate that not all bacterial populations are becoming highly resistant to antibiotics. This is particularly true of organisms from outdoor areas. However, organisms from certain hospital and clinic areas revealed patterns of increased resistance, while other hospital areas did not. Higher resistance to certain antibiotics which were used extensively was demonstrated for some antibiotics but not others. Air samplings

of a new hospital before and at periods after occupancy revealed increasing resistance in the population of the organisms. The findings suggest that the microbic population in some hospital areas not only reflects the antibiotics in use but may also represent a residual antibiotic-resistant flora remaining after the susceptible flora has been destroyed or eliminated. This flora may become a reservoir of potentially dangerous invaders for patients, and it is suggested that this reservoir in the hospital environment represents the most important source of resistant organisms[96]. Goldberg and Masterson undertook a study to determine the change in antibiotic sensitivity of *M. pyogenes* isolated from non-hospital personnel when they become hospital personnel. Prior to their entering hospital work, five to eight percent of the group of nursing students carried penicillin-resistant staphylococci. Within four weeks of assuming hospital duties 50 percent of the group became carriers of resistant cultures. This rate maintained itself throughout the eight months of the study[97].

ANTIBIOTIC FROM SEED PLANTS. Dull and his co-workers reported that a neutral oil derived from the leaf buds of *P. tacamahaca* yielded two sesquiterpene alcohols, one of which was identified as one of the isomers of bisabolol. This substance inhibited *M. tuberculosis,* strain H37, *in vitro* at a concentration of 5 micrograms per milliliter and also showed marked antagonism to other bacteria and to some pathogenic fungi. The other sesquiterpene alcohol, which so far remains unidentified, has similar antibiotic properties. These two compounds appear to be the substances primarily responsible for the antibiotic activity of the oil of the balsam poplar while part of the activity is due to cinnamic acid derivatives[98].

BACTERIAL SENSITIVITY. Waisbren presented a paper on the clinical applications of an analysis of the sensitivities of gram-negative bacilli to the antibiotics. He determined, through studies by the tube dilution method, the sensitivities to antibiotics of 410 strains of gram-negative bacilli that were isolated from infected patients. The data was presented and arranged in a manner found to be of maximum use to the clinician confronted with a patient who has to be treated without the results of sensitivity tests or even without a knowledge of the specific causative gram-negative bacillus. Successful treatment usually may be instituted on a basis of a precise knowledge of the relative activity of the antimicrobial drugs against each of the species of common bacteria and a knowledge of which antibiotic is likely to succeed after another has failed[99].

Culbertson reported a 12 year study of the comparative bacterial acquired resistance to the different tetracylines and chloramphenicol. Periodic summaries indicate that the percentage of bacteria which are sensitive to chloramphenicol has remained relatively constant whereas the incidence of bacteria which are sensitive to the tetracyclines has shown a slowly progressive decline[100].

Regarding bacterial sensitivity, Hsie and co-workers made an evaluation of the sensitivity of common pathogenic bacteria to various antibiotics. Two hundred and sixty-two strains of the common pathogenic bacteria isolated from January 1955 to June 1956 were tested against ten commonly used antibiotics and two nitrofuran derivatives by the disc method. Chloramphenicol still retains its place as the antibiotic with the highest overall efficacy. Furadantin and Furacin proved to be the next most effective drugs in combating the common pathogenic bacteria. Polymyxin B remains the most effective drug for *Pseudomonas aeruginosa.* Bacterial cross-resistance to the three tetracyclines and the two nitrofuran derivatives was not always consistent. Bacterial strains resistant to erythromycin and carbomycin were increasing out of proportion in view of the fact that the medication of erythromycin and of carbomycin was 1/26 and 1/78 the frequency of penicillin medication. This particular phenomenon is partly explained by the different patterns of the development of resistance to these three antibiotics[101].

POLIO VIRUS. Hollinshead and Smith reported a study on the effect of certain sulfur-containing compounds on the multiplication of poliomyelitis virus in tissue culture. From a total of 400 sulfur compounds studied for their inhibitory effects on poliomyelitis virus in tissue culture, five thiophene derivatives, four sulfones, five phenoxathiins, and five aliphatic compounds were the most effective. The phenoxathiin and aliphatic derivatives were virucidal. The thiophene derivatives caused the most marked delay of virus appearance. The viristatic activity of some of the thiophene compounds was reversed by hydroxyproline, cysteine, phenylalanine, tyrosine, methionine, and histidine; some of the sulfones were reversed by glutamine, and some of the aliphatic compounds were reversed by ethanolamine and betaine[102].

HISTOPLASMOSIS. Lehan and co-workers reported on therapeutic trials with the newer antifungal agents. The major portion of the study was devoted to the treatment of acute or chronic progressive histoplasmosis. Preliminary results on two new drugs, amphotericin B (Squibb) and Amebacide (Lilly) 1, 2 bis [p(n-hexyl methylamine methyl) phenoxy] ethane dihydrochloride), indicate that these two agents are relatively nontoxic, potential, *in vivo* antifungal agents[103].

Mycobacterium kansasii, or the "yellow bacillus" produces a disease in humans similar to typical tuberculosis. The sensitivity of *M. kansasii* to streptomycin, isoniazid, and para-aminosalicylic acid was studied in solid and liquid media. There was no statistically significant difference between the concentrations of streptomycin which cause inhibition of *M. kansasii* and *M. tuberculosis,* respectively. On the other hand, it required nine times as much para-aminosalicylic acid and 20 times as much isoniazid to cause inhibition of *M. kansasii* as to cause inhibition of *M. tuberculosis.* Streptomycin is the drug of choice in the treatment of this disease[104].

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notes on hospital pharmacy in the

Royal Navy in the 18th Century

by DAVID L. COWEN

IN THE EIGHTEENTH CENTURY, one Dr. James Sheilds, in compiling a list of prescriptions in use in Sir Guy's Hospital, took occasion to explain the need for pharmacists in general hospitals. Although, in something of an afterthought, he recognized the need of hospitals to "vary from the common officinal Prescriptions," his major contention was that hospitals needed their own pharmacists in order to overcome the "detestation and aversion" in which the general apothecary was purportedly held. As Dr. Sheilds wrote, the Apothecaries used:

> Tricks & mean Arts to adulterate Medicines, on purpose that they may come cheap to them, & yet abate nothing of their charge & price depreciation. Hence it is that private and public Hospitals secure genuine Medicines to themselves by having an apothy. belong to the said Hospitals.[1]

This deprecation of the Apothecaries' "vanity to act in both [i.e., both medical and pharmaceutical] Capacities," rather than to be "mechanic operators under the Physicians,"[2] is a familiar enough story. Here, however, the role of hospital pharmacy in hastening the separation of pharmacy from medicine becomes evident.

In Army installations, this separation does not seem to have taken place in the eighteenth century. The pharmacist's functions were apparently carried out by "Purveyors" who had "charge of the Medicines & Hospital Stores,"[3] and by Apothecaries. When new appointments were to be made, the former were to be selected from qualified "Senior Staff, or Regimental Officers"; the latter were "to be selected from the Assistant Surgeons, or Hospital Mates."[4] (All Mates were required to pass an examination for "Surgeon of a Regiment before the Court of Examiners at Surgeons Hall."[5]) Moreover, the War Office "Instructions for the Conduct of the Medical Staff to be employed on foreign Service" in "General as well as Regimental Hospitals" (1795) provided as follows with regard to the Apothecary:

> The Apothecaries are to have the immediate care of the Medicines attending to the issue of them according to the requisitions of the Physicians, or Surgeons, as the respective cases may require. And they are to act as Surgeons, as well as attend Patients under the care of Physicians should the necessity of the Service require their Assistance and should they be properly qualified to Act in both or either of those Lines. They are to see the Medicines properly compounded by the Hospital Mates and duly administered by the Subordinate Agents; and to prevent all waste: They are to give such advice and assistance in Compounding the Medicines as may be necessary and to make early requisitions for further Supplies before the former Stock of Medicines is exhausted.[6]

Office of Dispenser

In the Royal Navy, however, the process of professional particularization was begun early in the eighteenth century in the Hospitals for the Care of Sick and Wounded Seamen. Here there emerged the office of "Dispenser" at least as early as the year 1713. As of that year (1712/13) the name of Henry Blakey appears as Dispenser of Greenwich Hospital.[7] From then on, and for the remainder of the century, there are frequent references to the office in the records of the Royal Navy.

While it was true that Surgeon's Mates might be required to take on the duties of Dispenser,[8] and at times the Dispenser might be required to undertake the role of Surgeon's Mate,[9] the Dispenser was primarily a pharmacist and his duties pharmaceutical. Indeed, and most significant, the Royal Navy apparently proceeded on the principle (as stated in 1794) that "The Subordinate part of the Medical establishment is divided into three branches namely, that employed in assisting the Physicians, that employed in assisting the Surgeons, and that employed in compounding Medicines."[10] It is not surprising,

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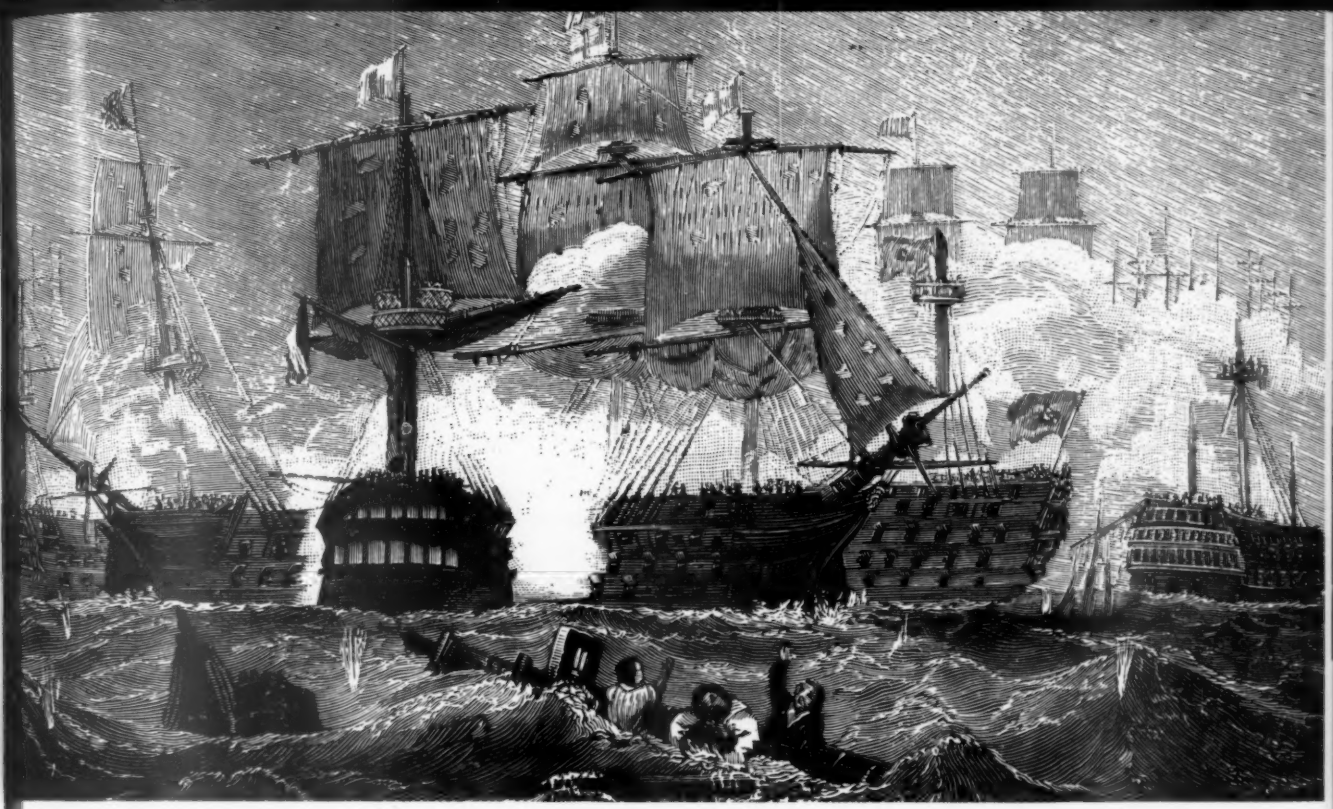


The battle of Trafalgar

then, that the Dispenser was specifically forbidden (1755) "to administer or apply any Medicine either internally or externally . . . without a written order from the Physician or one of the Chief Surgeons."[11]

The duties ascribed to the Dispenser clearly support this doctrine of separation. The earliest description of these that this writer has seen is to be found incidental to a 1740 Report on the Case of Sir James Barcley, Surgeon and Agent at Gosport.[12] Among the charges levelled against Sir James were "That he had not taken due Care to have the Medicines properly dispensed,"[13] and that he had not properly supervised the dispensary and the Dispenser. In the course of this investigation the following charge against the Dispenser was made, significant here as a description of the essentially pharmaceutical function of the Dispenser:

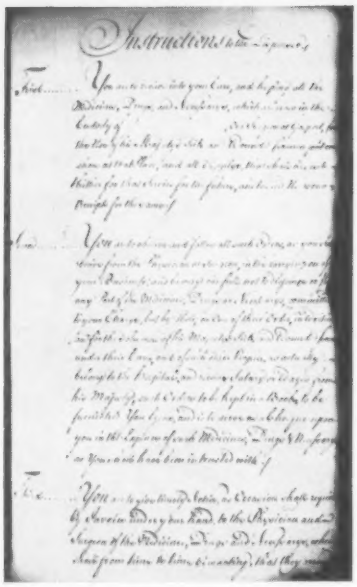
> As to Medicines, the Dispencers employ'd seldom observed the prescriptions given them, were negligent in Compounding, having no regard to Weight or Measure, and daily gave Medicines directly Contrary to what were prescrib'd.[14]

Not only was the Dispenser accused of doing things by guess, but there was some difference of opinion as to whether or not there actually were measuring instruments in the dispensary. One witness claimed that he "never saw any Weights, Scales, or Measures there";[15] another that he had seen them in the dispensary, "But they were so seldom made use of, that they were never hardly to be found."[16] Sir James himself admitted that he supposed "Scorbutic, Electuarys, Itchy Ointments, and Antifibrific Powders might be done [without measuring] without any prejudice to the patient."[17] Moreover, the Dispensers were accused of refusing Medicines when applied for, so that "Patients might sometimes have improper things,"[18] and that "very often Stinking bad Medicines [were] made use of."[19] (Perhaps this last referred especially to the oily mixtures, which the Dispensers were accused of forgetting to shake properly.[20])

Sir James contended that the charges were really against the Dispenser and not against himself,[21] and that, after all, he had to "trust to the Fidelity and Diligence of the Dispensers." Moreover, there had been no trouble while one Burford had been alive, he lamented, but "Humphrys, who Dispenced after him, was a regular bred Apothecary, but being Addicted to Drink, did not answer."[22]

(It is interesting to note that originally the medicines were kept in Sir James' "Own Bed Chamber,"[23] and, probably in October, 1740, "The Dispensary for the Town Quarters" was set up "in a Backwashhouse of the said Sir: James Barcley's House in Gosport."[24])

It was perhaps as a consequence of these deplorable conditions that the Lords Commissioners of the Admiralty requested, in 1742,[25] that the



USED WITH PERMISSION OF THE PUBLIC RECORDS OFFICE, LONDON

First page of draft of Instructions to the Dispenser, 1742.

Commissioners for the Care of Sick and Wounded Seamen (hereafter referred to as the "Commission") prepare a set of Instructions for hospital officers. At least there is evidence that the status and duties of the Dispenser were a prime consideration in developing these Instructions. First, the Commission, in submitting a draft of the Instructions to the Admiralty for approval, stated that "We shall be glad to know it [i.e., approval or suggestions for change] as soon as suits your Convenience, because We shall then immediately appoint the Dispensers and their Assistants at Portsmouth and Plymouth."[26] Second, the Instructions seem extremely pointed not only in outlining the duties of the Dispenser, but also in specially detailing the duties of the Physicians, Surgeons, and Agent *vis-à-vis* the Dispenser. (The importance of the Dispenser is indicated by the fact that the third article of the "Joint Instructions"[27] to the three officers made it mandatory for them, immediately upon the death of a Dispenser, to jointly take an inventory of the deceased's supplies, in the presence of the Assistant Dispenser, and to get a receipt therefor from the latter.)

More important, the Physicians and Surgeons were jointly required to transmit orders for medical supplies, upon their approval of invoices initiated by the Dispenser, and to examine and accept or reject the medicines when they arrived. They were particularly directed "never to permit the Dispenser to demand a Supply of any thing, which can be made or prepared by himself." This, be it noted, was premised on the assertion that "the Dispenser, and his Assistant are Men, who have been bred Apothecarys, and must therefore be capable of making and Compounding all things usually made and Compounded by People of that Profession."

Duties of Dispenser

In total, the supervision of the hospital pharmacy was in the joint hands of the Physician and Surgeon:

> They are to be very Carefull that the Dispenser and his Assistant do faithfully and Dilligently acquit themselves of their Business, in all respects; and for this end, frequently to Visit the Dispensary, & inspect their Conduct There; particularly in point of preserving, making, dispensing and Issuing the medicines &c.

The duties of the Dispenser were spelled out in detail:

> First . . . You are to receive into your Care, and keeping all the Medicines, Drugs, and Necessarys . . . which are now . . . at Gosport . . . and all Supplys, that shall be sent thither . . . for the future . . .
>
> Second . . . You are to observe and follow all such Orders, as you shall receive from the Physician or Surgeon, in the carrying on of your Business; and be very carefull not to dispense or issue [?] any Part of the Medicines, Drugs, or Necessarys committed to your Charge, but by their, or One of their Order, in Writing and for the sole use of his Majesty's Sick and Wounded Seamen, . . . and of such other People, as actually belong to the Hospital . . . such Orders to be kept in a Book . . . [which] is to serve as a Cheque upon you in the Expenses of such Medicines, Drugs & Necessarys . . .
>
> Third . . . You are to give timely Notice, as Occasion shall require, by Invoice under your hand, to the Physician and Surgeon of the Medicines, Drugs, and Necessarys, which shall from time to time be wanting, that they may adjust and Transmit the same to Us in Order to be supply'd.
>
> Fourth . . . You are to be very careful never to make a Demand of any Medicine, which You and Your Assistant, as having been bred to Pharmacy, are capable of making and compounding yourselves; and as all good Husbandry out [ought] to be Study'd and practiced, in this Part of His Majesty's Service . . . You are not to fail of making & preparing such Compounds, as shall be wanted from Time to Time, according to the Orders You shall receive . . . and to keep a Journal thereof in a Book . . . entering therein from time to time the Quantitys of Drugs &c which You shall convert or use in the making of Medicaments, and the Quantitys so made.
>
> Fifth . . . You are at the end of every Year, or oftener, if We require it, to make Oath . . . that you have not . . . dispensed, Issued, or used, or suffered to be dispensed, Issued, or Used, and Medicine, Drug, or Necessary . . . but according to the Orders, You had received for that Purpose from Our Physician or Surgeon, and for the People entituled to the Benefit thereof.
>
> Sixth . . . Whenever You are Order'd by the Physician and Surgeon, to deliver any Parcel of Medicines, Drugs or Stores to any Mate or Assistant to the Surgeon, for the Use of such Sick and Wounded . . .

particularly committed to their respective Care, by reason of their great Distance from your Dispensary, you are to take Receipt at the Foot of the Order for them, and reserve the same for your own Justification . . .

Assistant Dispenser

In addition, instructions to the "Assistant Dispenser" made the latter subject to the orders of the Physician, Surgeon, or Dispenser, required of him the same sort of oath required of his immediate superior, and put him on warning that in the event of the death of the Dispenser, custody of the supplies would devolve upon him.

Medical Supplies

In 1755, a revised set of Instructions for Haslar Hospital,[28] though essentially repeating the earlier Instructions, was more specific or more stringent in several particulars. The Dispenser's responsibility for keeping up supplies was made more emphatic, and the Dispenser could procure, by his own written order, and with some discretionary power, such necessaries as were available from the Agent at Portsmouth or Gosport. He was required to notify the Physician of new deliveries so that the latter might make his inspection. His records of "the prescriptions or orders" were now to be kept "in a separate Book or on File," but his clerical duties were greatly enhanced with the assignment to him of what were essentially the duties of a hospital registrar:

He is duly to enter into a Book . . . the Names of all the Physicians proper Patients particularly with regard to their diseases times of admittance and those of discharge.

Again the demands of good husbandry were evident. This time not only was the Dispenser importuned not to "demand any sort of medicines which may be made or compounded in the Dispensary," but he was warned to be "as frugal as the service will admit" in his orders, and, in a special instruction, he was directed:

to be careful to save all Glasses Potts &c [?] served into the Dispensary that so after they are emptied they may again be made use of upon future occasions.

The Dispenser and his two Assistants were required to make their oaths quarterly, instead of annually, and the former was empowered to allow the latter "a day or two's absence . . . upon extraordinary occasion." The last may seem trivial enough, but, together with the more responsible and discretionary powers mentioned above, indicates that the Dispenser was attaining a higher status in the hospital service. It must also be remembered that it was these Instructions that included the stricture, already mentioned, against the administration of drugs by the Dispenser.

The impact of these 1755 Instructions was probably not too great, however, for in the 1790's it was the Instructions of 1742, not those of 1755,[29] that were re-stated. Thus the "Instructions to Mr. William Richardson Dispenser of Medicines, Drugs, and Necessaries to Sick & Wounded Seamen and Marines at the Royal Hospital at Haslar, Gosport,"[30] were almost a verbatim copy of the 1742 Instructions. (There is a plaque in memory of this Mr. Richardson in the Hospital Chapel.[31]) Similarly, a year or two later, Instructions from the Admiralty to the Commission, followed the 1742 pattern with regard to the Dispenser, often, in fact, incorporating the same phraseology.[32]

Examination of Medicines

Such formal statements of "Instructions," however, cannot of course detail all of the activities of the Dispenser. For example, although nowhere in the Instructions is it even suggested that the Dispenser was permitted to "view" drugs, that is, to examine them as to their quality, the Commission directed (1757) that the supplies for the Hospital Ship *Thetis* be viewed by the First Surgeon and Dispenser of the Haslar Hospital and the Surgeon of the *Thetis*.[33] This was indeed a concession to the standing and ability of the Dispenser. (In 1808 the "Commissioners appointed for Revising the Civil Affairs of His Majesty's Navy" recommended that the Surgeon in naval hospitals abroad be required, "in conjunction with the Dispenser," to examine all medicines received as to their quality and quantity.[34])

Perhaps even more important, were the regulations imposed on the Dispenser by the Physician. The earliest set of such rules which this writer has seen has been attributed to Dr. James Lind (at Haslar from 1758-1783),[35] and certainly reflect the abilities of that outstanding figure in naval medicine. A pharmacopoeia for the hospital (ascribed to Lind) included the following statement of precautions to be taken in dispensing, and represent a very early exposition of such techniques:

To prevent the dangerous consequences of patients' receiving wrong medicine from mistakes in dispensing them, every basket is to be inspected after the medicines are put up, and the medicines in it compared with the prescription ticket of each patient; the Dispensing cheque, a line, being drawn upon the ticket under the name of each medicine or called over and put into the basket.[36]

Moreover, it was required that:

Every medicine sent up to the Wards is to have a label upon it containing the name of the medicine and

of any addition made to it, the direction for taking it and the patients' name, not abbreviated but distinctly wrote out in words at length.[37]

Finally, it was required that "Medicines of great efficacy when repeated are always to be expressed with words at length," although this rule was not practiced after Lind's incumbency. (Instead, prescriptions were repeated under a letter classification.)[38] This "caution against the use of wrong medicines" seems to have continued as a recognized responsibility of the Dispenser, for such rules were again spelled out in some details in Instructions proposed for naval hospitals abroad in 1808.[39]

Qualifications

The successful carrying on of these duties by the Dispenser of course required that, as suggested in the Instructions, they be "bred Apothecary," or "bred to Pharmacy." There is some proof, other than the reference to the alcoholic Humphrys, that this was the case. For example, at a meeting of the Court of Assistants of the Society of Apothecaries held on May 9, 1755, it was reported that:

> Mr. James Shannon was examined touching his Knowledge in Pharmacy (pursuant to a Letter for that Purpose from the Honourable Commissioners for Sick and Wounded Seamen) and found qualified to act as Dispenser to his Majesty's Hospitals for the Navy and a Certificate thereof signed by the said Committee.[40]

Similarly, in 1761 the Commission recommended a Mr. Cornwall for Dispenser at Barbadoes (or Antiqua); Mr. Cornwall had passed an examination at the Apothecaries Company "Who have certified to Us that they find him qualified for the Employment for which he is named."[41] Again in 1779, one Hugh Wynn was examined "touching his Qualification for an Assistant Dispenser" (for Haslar) and found "well Qualified for that purpose."[42] Finally, in 1793, the Commission recommended the promotion of John Shapcote, who had "passed an Examination at Apothecaries Hall," from Assistant Dispenser to Dispenser.[43] These were probably not the only such cases, but it is significant that the examinations in these four instances were really touching upon the qualifications of these men as *pharmacists,* not as *apothecaries,* as the latter term was understood in England.

On the basis of such standards, and the Instructions, it is to be expected that the conditions described in the Barcley case in 1740 were corrected. In any case, in 1766 the Commission requested the Admiralty's permission to make up Robert Stowe's Quintessence in the hospital dispensaries rather than purchase it from Mr. Stowe. In the dispensaries not only would there be the supervision of Dr. Lind, the Commission pointed out, but the "ability and fidelity of our Dispensers," could be depended upon.[44] At the end of the century, however, Thomas Trotter, Physician to His Majesty's Fleet, asked for a second dispensary at Haslar, contending that:

> The present one is on too confined a scale for the whole business. In a full hospital the work of this shop is by much too great for the room, and also for one person to superintend . . . During the hours of employment, I have seen the gentlemen of Haslar Dispensary working more like porters than apothecaries.[45]

But Dr. Trotter also pointed out that "If there is any virtue in the practice of physic, too much attention cannot be paid to the composition of articles of medicine: if the accuracy of composition is not attended to, the whole fabrick of hospital charity is destroyed, as the sole purpose of an hospital is to cure diseases."[46] In a similar vein, a year earlier, Admirals Caldwell and Gardner, in a report on an inspection of Haslar Hospital, had referred to the Dispenser's office as one "of considerable trust and importance."[47]

Except for the personnel of hospital ships, where Surgeon's Mates acted "one as Dispenser, the other as Assistant Dispenser, besides their duty as Surgeon's Mates,"[48] the office of Dispenser, separate from the other medical personnel, apparently made its way generally into naval hospital installations. (It is also noteworthy that the *Medical Register for the Year 1779* indicates that no hospital other than the naval installations listed "Dispensers"; general hospitals listed "Apothecaries.") In 1746 a Dispenser and an Assistant Dispenser were reported at Greenwich Hospital.[49] In 1779, both were still listed among the medical personnel at Greenwich, the hospital at Plymouth also reported a Dispenser and an Assistant; and Haslar boasted a Dispenser and six Assistants.[50] By 1794 the last number had been increased to eight, and it was recommended that two more be appointed (there were at the time some 1300 patients at Haslar, and plans for the hospital as a war establishment caring for some 1200 patients called for one Dispenser and seven Assistant Dispensers, and on a peace basis caring for 550 patients, one Dispenser and four Assistants).[51] In 1797 there was a Dispenser and five Assistant Dispensers at the hospital for prisoners of war at Norman Cross.[52] In 1761 Dispensers were included in the plans for installations at Barbadoes and Antigua,[53] and, in 1793, in the plans for a hospital for prisoners at St. Christopher.[54] As a matter of fact, the Instructions of 1795-96 spoke not only of "Dispensers at the established Hospitals at Home," but also of the "Dispensers abroad."[55]

Instructions proposed for hospitals abroad, in 1808, included instructions for only three officers: Surgeon, Agent, and Dispenser.[56] Indeed, those for the last, although they reflected eighteenth century practices, seem to indicate that the Dispenser had even greater responsibilities abroad than at the hospitals at home.[57]

The position of Chief Dispenser was "considered as a situation for life,"[58] and Henry Blakey seems to have held the position at Greenwich for at least thirty-three years (1713-1746) and perhaps forty-four (1713-1757).[59] In 1794 the Dispenser at Haslar was recommended for superannuation at the age of seventy-three.[60] The position of Assistant Dispenser, however, showed no such stability: "great inconvenience arises from frequent changes—especially in the Dispensary," ran the complaint in the same year.[61]

Salary

Part of this difference in stability was probably the result of the salaries paid. While the Chief Dispenser at Greenwich was reported, in 1789, to be receiving only £50, the Assistant received but £30 (the Surgeon received £150 and the Physician £182/10/0) per annum.[62] (In 1746 Blakey had been reported to be receiving a salary of £60 per annum.[63]) The Dispenser at Haslar was paid £100 in 1763 and the Assistant only £50. (The Physician received £200 and the Surgeon £150.)[64] In 1794 the salary of the Chief Dispenser at Haslar was still £100. This was considered too small by the Admiralty investigators, as indeed it would be if their recommendations that the Assistant Dispenser receive a per diem of 5s. and a Principal Assistant (who had to be "always present, night and day") a per diem of 6s., were to obtain.[65] (The former was calculated, apparently for a full 365 day year, at about £92, at which rate the latter would be over £109.) By the end of the century, however, the Chief Dispenser at Haslar was receiving £150.[66] (At Haslar, at this time, six officers were permitted to "feed cattle . . . on the hospital airing and burying ground." Two cows were permitted each of the four principal officers, and one each for the Dispenser and Chaplain.)[67]

The Dispenser and at least some of his assistants were usually accorded residence at the hospital. Special arrangements for "apartments" were made for them, along with other medical officers, when the Infirmary was built at Greenwich in 1763 or 1764.[68] At Haslar, in 1794, the Dispenser and his Assistants, among others, occupied "Several Wards & Cabins," and it was proposed that separate apartments be provided for them "within or immediately without the walls of the Hospital."[69] Thus needed space would be released for the sick,[70] and these officers would be less likely to be "exposed to infection from living and sleeping in the Hospital."[71]

Role of Apothecaries

It is perhaps not necessary to point out again that the "Dispenser" was essentially a pharmaceutical operator and quite different from an "Apothecary." The Apothecary was not unknown in the Royal Navy Hospitals, and although the terms "Dispenser" and "Apothecary" seem sometimes to have been used without distinction,[72] the latter was essentially a medical practitioner, not a pharmacist. Thus, in 1758, James Lind, recommended an increase in the number of apothecaries at Haslar where there were then one apothecary and two assistants, "as these . . . are to be appropriated to visit with the Physicians in the Wards."[73] These were usually called "Visiting Apothecaries," and seem to have played as anomalous a role in the Navy as they were playing in public life, for, in 1783, the Commission asked, apparently without success, that the services of two Visiting Apothecaries appointed by the Admiralty to Haslar Hospital (at £100 p.a. and £18/5/0 for house rent) be dispensed with.[74] In 1795, however, Dr. Trotter was asking for nine Visiting Apothecaries at Haslar and five at Plymouth.[75] Trotter gave the following description of the function of these apothecaries:

> A visiting apothecary ought to reside in every pavilion, to superintend the administration of medicines, all the wards of which should be submitted to him. To assist him in this business, a labourer at 1s.6d. per diem, should also reside on the spot. who might occasionally assist the nurses, and bring the medicines, &c. from the dispensary. The physician would, by these means, have more regular reports given him of the state and condition of his patient, and it would serve to bring the whole to a more perfect system of practice.[76]

But the most pointed and interesting comment on the Apothecary was made in the course of the Admiralty investigation of 1794:

> There are at present what are improperly called Visiting Apothecaries, who are attached to the Physicians with a Salary of £100 p Annum, It is proposed that one of these shall continue to assist each of the Physicians under the name of principal Medical Assistant.[77]

Almost fifty years later (1841) the Apothecaries Society was to issue a statement remarkably similar:

> . . . one of the chief evils of the present position of the Apothecary is his name, which has little reference to his actual duties, that he is in fact the Medical Attendant on the larger mass of the community, and should be designated the General Practitioner of Medicine.[78]

Thus, in conclusion, this study points up not only the fact that the Royal Navy seemed to accomplish in the eighteenth century what the medical profession had failed to accomplish by legislation and court decision: the restriction of the pharmacist to his peculiar function; but also the fact that the Navy, in putting the "Apothecary" into his place as a medical practitioner, was aiding the process whereby the field of pharmaceutical practice was to be left to the Chemists and Druggists in public life. The tendency, however, apparently did not take firm root, for it did not blossom in the next century. For example, although the proposed instructions for Dispensers at foreign stations, in 1808, provided that "You are to confine the practice of your profession, strictly and exclusively to your public duty . . . and you are, on no account, to visit, attend, or prescribe for any Patient, in or out of the Hospital," the same instructions called upon them, "when the business of the Dispensary will admit of it" to assist the Surgeon "in visiting the physical, or in dressing the surgical Patients."[79] In 1819 "The Present Establishment of Officers" at Greenwich Hospital listed an "Apothecary and one Assistant" but no "Dispenser."[80] And, finally, from 1831 to 1870 the "Dispenser (at Haslar) was replaced by a "Surgeon in Charge of Stores."[81] Only since 1872 has the position been held by a regular pharmacist, first under the old title of "Dispenser" (until 1916), and thereafter as "Pharmacist."[82]

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1. Ms. of Dr. James Sheilds (n.d.). British Museum, (Printed Books T475/3), pp. 2-3.

2. *Ibid.*, p. 2.

3. "Memorandum relative to a Medical Staff for Jamaica" (c. 1781). *War Office, Miscellaneous Statistics,* 1776-1783 (Public Record Office, W. O. 1/890), f. 196, 196v.

4. "General rules relating to the qualifications for appointments in the Medical and Chirurgical Branches of the Service . . ." Mar. 12, 1798. *War Office, Miscellany Book, 1797* (P.R.O., W. O. 26/37), p. 362.

5. *Ibid.*, p. 361.

6. *War Office, Miscellany Book,* 1795-1796 (P.R.O., W.O. 26/36), p. 48.

7. *An Historical Account of the Royal Hospital for Seamen at Greenwich* (London, 1789), p. 141, lists the names of only Blakey and John Pocock, the latter with the date 1757 before his name. *The Laws, Ordinances and Institutions of the Admiralty of Great Britain* (London, 1746), vol. 2, p. 398, lists Blakey as the Dispenser "belonging to his Majesty's Royal-Hospital at Greenwich," and Edward Grace as his assistant. The 1767 printing of this work makes the same citations, but since it is apparently an exact reprint of the 1746 edition, its personnel lists can hardly reflect the 1767 situation.

8. In 1740, John Ailway, Surgeon's Mate, was assigned "as Dispenser of Medicines to Sir James Barcley Bar . . .—for about one Month" at Gosport. "Affidavit of John Ailway," Nov. 16, 1740. *Admiralty, In-Letters from Medical Department, 1741-1742* (P.R.O., Adm. 1/3529).

9. During the illness of a Mate, the Dispenser at the Hospital at Gosport, Robert Waller, undertook to bleed and dress, as well as dispense medicines, without pay, "for the sake of Improving himself." "Copys of Sir James Barcley's Observations on the Affidavits of Mr. Fidge, Ailway & Waller," (n.d.), *ibid.*

10. "Supplement to the Report on Haslar Hospital" (1794). *Admiralty, In-Letters from Medical Department, 1793-1800* (P.R.O., Adm. 1/3533).

11. "Instructions to be observed by the Physician, Surgeons and other Officers &c [?] of His Majesty's Hospital at Haslar," July 3, 1755, *ibid.*

12. The recent celebration of the Bicentenary of the Hospital at Gosport (See, "Two Hundred Years of Naval Pharmacy," *The Chemist and Druggist,* 1953, vol. 159, p. 586) was a celebration of the opening of the building; "hospital" provisions at Gosport began much earlier, probably about 1713. Cf., J. Glass, "James Lind, M. D. Eighteenth Century Naval Medical Hygienist," *Journal of the Royal Naval Medical Service,* 1949, vol. 35, p. 78.

13. Commissioners for the Care of Sick and Wounded Seamen to the Lords Commissioners of the Admiralty [Hereafter in these notes the former will be referred to as "Commission" and the latter as "Admiralty"], Mar. 6, 1740. *Admiralty, In-Letters from Medical Department, 1741-1742* (P.R.O., Adm. 1/3529).

14. "Letter and Affidavit of Mr. Carlos," Feb. 27, 1740 [1740/41], *ibid.*

15. "Affidavit of William Fidge," Nov. 12, 1740, *ibid.*

16. "Affidavit of Robert Waller," Nov. 11, 1740, *ibid.*

17. "Sir James Barcley's Answer to the Affidavits delivered by himself," Dec. 10, 1740, *ibid.*

18. Commission to Admiralty, Mar. 6, 1740, *ibid.*

19. Affidavit of William Fidge," Nov. 12, 1740, *ibid.*

20. "Sir James Barcley's Answer to the Affidavits delivered by himself," Dec. 10, 1740, *ibid.*

21. "Sir James Barcley's Answer to the Affidavits sent to the Board," Nov. 20, 1740, *ibid.*

22. "Sir James Barcley's Answer to the Affidavits delivered by himself," Dec. 10, 1740, *ibid.*

23. *Ibid.*

24. "Affidavit of William Fidge," Nov. 12, 1740; "Affidavits of Robert Waller," Nov. 11, 1740; and "Sir James Barcley's Answer to the Affidavits sent the Board," Nov. 20, 1740; *ibid.*

25. On Feb. 16, 1741/42. Commission to Admiralty, June 3, 1742, *ibid.*

26. *Ibid.*

27. "Instructions to be Observed by their Officers . . . Joint Instructions to the Physician, Surgeon, and Agent," Draught dated June 3, 1742, *ibid.* The quotations that follow are from this Draught, including the "Joint Instructions to the Physician and Surgeon," and the "Instructions to the Dispenser," and the "Instructions to the Dispensers Assistant."

28. "Instructions to be observed by the Physician, Surgeon and other Officers &c [?] of His Majesty's Hospital at Haslar," July, 1755, *loc. cit.*

29. Oddly, the 1755 Instructions are not found in their chronological place in the Admiralty papers. They follow the Richardson Instructions and the Caldwell-Gardner Report in a volume dated 1793-1800. The

signatories of the document, however, established the fact that "1755" is not a clerical error.

30. Dated July 7, 1794. *Admiralty, In-Letters from Medical Department, 1793-1800* (P.R.O., Adm. 1/3533). 33).

31. "Two Hundred Years of Hospital Pharmacy," *loc. cit.*, p. 586.

32. "Proposed Instructions to the Commissioners for Sick and Wounded Seamen" 1795-1796. *Admiralty, Medical Department, Out-Letters, 1796-1797* (P.R.O., Adm. 98/18), pp. 83, *et seq.*, especially pp. 102-105.

33. Commission to Admiralty, Dec. 13, 1757. *Admiralty, Medical Deparment, Out-Letters, 1757-1759* (P.R.O., Adm. 98/7), p. 68.

34. *Instructions for the Naval Hospitals on Foreign Stations as Proposed by the Commissioners appointed for Revising the Civil Affairs of His Majesty's Navy,* (London, 1809), Instructions to Surgeons, p. 18; and Instructions to Dispensers, p. 3.

35. "Two Hundred Years of Hospital Pharmacy," *loc. cit.*, p. 586.

36. As quoted, *ibid.*

37. As quoted, *ibid.*

38. As quoted, *ibid.*, pp. 586-587.

39. *Instructions for Naval Hospitals on Foreign Stations . . .* , Instructions to Dipensers, pp. 5-6.

40. *Society of Apothecaries Court Minute Book Fair,* vol. 8, 1745-1767 (Guildhall Lib., Ms. 8200/7), f. 132v.

41. Commission to Admiralty, Nov. 25, 1761. *Admiralty, Medical Department, Out-Letters, 1761-1763* (P.R.O., Adm. 98/9), p. 42.

42. *Society of Apothecaries Rough Court Minute Book,* vol. 13, 1776-1783 (Guildhall Lib., Ms. 8201/13), Meeting of Dec. 7, 1779.

43. Commission to Admiralty, Nov. 22, 1793, *Admiralty, Medical Department, Out-Letters, 1793-1794* (P.R.O., Adm. 98/16).

44. Commission to Admiralty, Apr. 28, 1766. *Admiralty, Medical Department, Out-Letters, 1764-1774* (P.R.O., Adm. 98/10), p. 146.

45. T. Trotter, *Remarks on the Establishment of Navy Hospitals and Sick Quarters with Hints for their Improvement* (n.p., 1795[?]), pp. 27-28.

46. *Ibid.*

47. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

48. Commission to Admiralty, June 14, 1797. *Admiralty, Medical Department, Out-Letters, 1796-1779* (P.R.O., Adm. 98/18), p. 242.

49. *The Laws, Ordinances and Institutions of the Admiralty of Great Briatin* (London, 1746), vol. 2, p. 398.

50. *Medical Register for the Year 1779* (London, 1779), pp. 76, 87, 93.

51. "Remarks made on an examination of the Royal Hospital at Haslar from the 28th March to the 4th April 1794 . . . by Rear Admirals Caldwell and Gardner . . . " March 27, 1794 [*sic*] *Admiralty, In-Letters from Medical Department, 1793-1800* (P.R.O., Adm. 1/3533); and "Supplement to the Report on Haslar Hospital" (1794), *ibid.*

52. Commission to Admiralty, May 26, 1797. *Admiralty, Medical Department, Out-Letters, 1796-1797* (P.R.O., Adm. 98/18), p. 236.

53. Commission to Admiralty, Sept. 3, 1761. *Admiralty, Medical Department, Out-Letters, 1760-1761* (P.R.O., Adm. 98/8), p. 475; and Commission to Admiralty, Nov. 25, 1761. *Admiralty, Medical Department, Out-Letters, 1761-1763* (P.R.O., Adm. 98/9), p. 42.

54. Commission to Admiralty, Nov. 22, 1793. *Admiralty, Medical Department, Out-Letters, 1793-1794* (P.R.O., Adm. 98/16).

55. "Proposed Instructions to the Commissioners for Sick and Wounded Seamen," 1795-1796, *loc. cit.*, p. 103.

56. *Instructions for the Naval Hospitals on Foreign Stations . . .*

57. The Dispenser was to be required to "assist the Surgeon in the duty of receiving Patients"; new patients were to be bathed "invariably . . . in the presence, and under the superintendence, of the Surgeon, yourself [the Dispenser] or an Hospital Mate"; the Dispenser was to be assigned many obligations in the outfitting of ships, etc.; *ibid.*, Instructions to Dispensers, pp. 2, 7, 10-11, 12-13.

58. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

59. See note 7 above.

60. "Remarks made on an examination of the Royal Hospital at Haslar . . . by Rear Admirals Caldwell and Gardner," Mar. 27, 1794, *loc. cit.*

61. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

62. *An Historical Account of the Royal Hospital for Seamen at Greenwich* (London, 1789), p. 82.

63. *The Laws, Ordinances and Institutions of the Admiralty of Great Britain* (London, 1746), vol. 2, p. 398.

64. W. Tait, *A History of Haslar Hospital* (Portsmouth, 1906), pp. 86, 87.

65. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

66. Tait, *op. cit.*, p. 100.

67. *Ibid.*, p. 54.

68. *An Historical Account of the Royal Hospital for Seamen at Greenwich* (London, 1789), p. 118.

69. "Remarks made on an examination of the Royal Hospital at Haslar . . . by Rear Admirals Caldwell and Gardner . . ." Mar. 27, 1794, *loc. cit.*

70. *Ibid.*

71. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

72. E.g., T. Trotter, *op. cit.*, pp. 20, 28.

73. Lind to Sir Alexander Dick, Sept. 3, 1758. Quoted by L. H. Roddis, *James Lind* (New York, 1950), pp. 128-129.

74. Commission to Admiralty, Apr. 7, 1783. *Admiralty, Medical Department, Out-Letters, 1781-1785* (P.R.O., Adm. 98/14), p. 342.

75. *Op. cit.*, p. 17.

76. *Op. cit.*, p. 19.

77. "Supplement to the Report on Haslar Hospital" (1794), *loc. cit.*

78. As quoted by E. Kremers and G. Urdang, *History of Pharmacy,* 2nd ed. (Philadelphia, 1951), p. 142.

79. *Instructions for the Naval Hospitals on Foreign Stations . . .*, Instructions to Dispensers, pp. 11, 13. It is worth noting that the Dispensers were to be forbidden "to keep, or in any way to be concerned in keeping, a shop for the sale of medicines, drugs, and other articles." *Ibid.*, p. 13.

80. *A Description of the Royal Hospital for Seamen at Greenwich* (London, 1819), p. 47.

81. "Two Hundred Years of Naval Pharmacy," *loc. cit.*, p. 586.

82. *Ibid.*

ABBREVIATED TITLES FOR *serological products*

by W. L. M. PERRY

AND

H. J. PARISH

NOTE TO HOSPITAL PHARMACISTS

Members of the British Pharmacopoeia Commission have proposed the adoption of a set of titles and abbreviations for serological products. It has been suggested that these titles and abbreviations be used in the U. S. PHARMACOPEIA *and in the* BRITISH PHARMACOPOEIA.

Members of the SOCIETY *are requested to review the suggestions contained in the accompanying article and to write their comments to Dr. Lloyd C. Miller, Director of Revision, Pharmacopeia of the United States, 46 Park Avenue, New York City* 16.

While the U.S.P. does not now include abbreviations of products in its monographs, Dr. Miller has asked whether the difference in the way serums, antitoxins, and vaccines are used is enough to justify a fundamentally different attitude toward them. Since the official serological products are used fairly widely in hospital practice, hospital pharmacists are requested to send their views and opinions of this proposal to Dr. Miller. Also, Directors of hospital pharmacy internship programs may wish to have their interns study this proposal in detail and prepare a recommendation for transmittal to Dr. Miller.

INCREASING EMPHASIS IS BEING PLACED on the availability of immunization and serotherapy records which should be accurate, brief, legible, and easily understood. While different manufacturers and doctors devise their own capital abbreviations or symbols for proper names or trade names, difficulties often arise if patients change their doctors in any one country, and the trouble is likely to be even worse if they move to another country. These difficulties have already been the subject of comment in the medical press.

As the number of preparations with lengthy titles—for example, some of the varieties of combined prophylactics—is increasing every year, it would be very desirable to agree either nationally, or preferably internationally, on abbreviations for such biological products. It is of considerable importance that the number of such abbreviations should be kept within bounds, and that a doctor should be able to identify correctly the materials mentioned in any records presented to him.

Examples of Confusion

This is far from the case at present, and there is evidence that symbols, both official and unofficial, have in practice given rise to confusion. Examples are as follows:

(*a*) A.T.T. may mean tetanus antitoxin, (A.T.S.) or tetanus toxoid (T.T.).

(*b*) A.D.S., D.A.T., A.T.D., C.D.A., and R.D.A. have all been used for diphtheria antitoxin. The C in C.D.A. stands for "concentrated" and the R in R.D.A. for "refined."

(*c*) T.A.B.C. usually indicates typhoid and paratyphoid A. B. and C vaccine, but some doctors use it for

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T.A.B. plus cholera vaccine. The Ministry of Health in this country issued a directive many years ago that "cholera" was always to be written in full in a vaccine title, but this ruling may not be generally known. T.A.B.T. is the usual abbreviation for T.A.B. vaccine and tetanus toxoid, but this combined prophylactic has sometimes been recorded as T.A.B.T.T. In some countries the final T of T.A.B.T.T. might be thought to imply typhus vaccine.

(*d*) D.T.P. indicates diphtheria-tetanus-pertussis prophylactic in some parts of the world, whereas in Great Britain it might be interpreted as diphtheria-tetanus prophylactic. This particular confusion is unfortunate, as it is important to know whether a young child has been protected against pertussis. Recently, yet another combination of letters—namely, C.D.T. (combined diphtheria and tetanus toxoids)—has been employed for diphtheria-tetanus prophylactic in Australia. Furthermore, W.D.P. and D.P.P. both stand for diphtheria-pertussis prophylactic in Great Britain.

(*e*) The French T.A.B.T.D.R. is a mixture of T.A.B. vaccine, tetanus and diphtheria toxoids, and typhus rickettsiae. Probably few people in other countries would identify the product correctly.

These few examples serve, we hope, to illustrate the confusion. Perhaps, as a last word, we may point out that the letter P, which often occurs in the abbreviations in current use, stands from time to time for purified, pertussis, precipitated, phosphate, or prophylactic.

Agreed Abbreviations

Confusion can only be avoided by the agreed adoption of a logical scheme of abbreviations. Such a scheme would require the approval, in any one country, of the controlling authorities, both legislative and pharmacopoeial. Thus, in Britain, official abbreviations would require approval under the Therapeutic Substances Act, and such approval could be endorsed by inclusion of the abbreviated titles in the appropriate monographs of the *British Pharmacopoeia*.

Obviously national agreement could be secured more easily than international agreement, the latter being, equally obviously, the final aim. Consequently, any scheme proposed for national use should as far as possible be designed in such a way—for example, by the abbreviation of Latin rather than English titles—that it can be readily adapted to international needs.

With these considerations in mind the Serological Products Committee of the British Pharmacopoeia Commission has been discussing the whole problem. No final proposals have yet been put forward by the Committee, and the suggested outline that we give below represents our own ideas. Nevertheless, the Committee felt that a useful purpose would be served by asking for comments on these preliminary and tentative proposals before any official action was taken, and has approved the publication of this note.

Outline of Proposed Scheme

The basic scheme which we suggest consists of two parts, each abbreviation comprising (1) a shortened version of the name of the disease or organism associated with the material administered, and (2) a shortened version of the name of the type of product concerned. In some cases a third part may have to be added in order to identify a particular variety of the type of product.

Names of Diseases or Organisms

The first general principle is that, where only one disease or organism is mentioned, three letters (usually the first three) are used. Wherever possible the Latinized title is abbreviated. Should confusion appear likely as a result of this general method of abbreviation, the full name is used. The following is a list exemplifying the system:

Cho =Cholera
Dip =Diphtheria
Gas=Gas gangrene (oedematiens+septicum+welchii)
Oed =Gas gangrene (oedematiens)
Sep =Gas gangrene (septicum)
Wel =Gas gangrene (welchii or perfringens)
Lep =Leptospirosis
Per =Pertussis (whooping-cough)
Pol =Poliomyelitis
Rab =Rabies
Sca =Scarlatina
Sta =Staphylococcus
Tet =Tetanus
Tub =Tuberculosis
Typhoid=Typhoid
Typhus =Typhus
Var =Variola (smallpox)
Yel =Yellow-fever

The second general principle is that, where more than one disease appears in the title, capital letters only are used as abbreviations for the names of the diseases and organisms. This is necessary in order to avoid overlong abbreviations, and, in our view, can be accomplished without confusion within the framework of this general scheme. Examples of such combined preparations and their abbreviated titles are given below.

TAB =Typhoid, paratyphoid A, paratyphoid B.
TABC=Typhoid, paratyphoid A, paratyphoid B, and paratyphoid C.
TABT=Typhoid, paratyphoid A, paratyphoid B, and tetanus toxoid.
DTP =Diphtheria, tetanus, and pertussis.

N.B.—Unless the use of a single letter (capital abbreviation) for each disease has been "recognized" for inclusion in the name of a given combined preparation, the first three letters of the disease should be employed, as, for example, in designating typhoid, paratyphoid A and B, and cholera vaccine as TABCho.

Type of Product

The abbreviation of the name of the disease or organism is followed by a diagonal line, after which appears the abbreviation for the type of product. The scheme envisages the use of two principal types of product—namely, prophylactics, for which the general abbreviation Vac is suggested, and therapeutic antisera, for which the general abbreviation Ser is suggested. In a few cases the abbreviation Vac will be replaced by Tox, where both a vaccine and a toxoid are commonly available. The following examples show how certain well-known products would be abbreviated according to this scheme.

Cho/Vac	=Cholera vaccine
Dip/Ser	=Diphtheria antitoxin
DP/Vac	=Diphtheria-pertussis prophylactic
DTP/Vac	=Diphtheria-tetanus-pertussis prophylactic
Sep/Ser	=Gas gangrene (septicum) antitoxin
Wel/Ser	=Gas gangrene (welchii) antitoxin
Gas/Ser	=Mixed gas gangrene antitoxin
Sca/Vac	=Scarlet fever prophylactic
Var/Vac	=Smallpox vaccine
Sta/Tox	=Staphylococcus toxoid
TABC/Vac	=Typhoid, paratyphoid A, B, and C. vaccine
TABCho/Vac	=T.A.B. and cholera vaccine
TABT/Vac	=T.A.B. vaccine and tetanus toxoid
Tet/Ser	=Tetanus antitoxin
Tet/Vac	=Tetanus toxoid

Varieties of Type of Product

Where there are a number of distinct varieties of one type of product and it is desirable to distinguish between them, the two-part abbreviation just described is followed by another diagonal line, after which is written an approved abbreviation for the particular variety of product concerned. This should not be a frequent problem and is of major importance only in the case of the diphtheria prophylactics. The following examples serve to illustrate how the scheme would work.

Dip/Vac/FT	=Diphtheria prophylactic formol toxoid
Dip/Vac/APT	=Diphtheria prophylactic alum precipitated toxoid
Dip/Vac/PTAP	=Diphtheria prophylactic purified toxoid aluminum phosphate
Dip/Vac/TAF	=Diphtheria prophylactic toxoid antitoxin floccules
Tub/Vac/BCG	=B. C. G. vaccine

It should be noted that it is only in these varieties of product—namely, in the third part of the abbreviation—that departures from the general principles that we have enunciated creep in because of well-established usage. Thus, P is used in Dip/Vac/PTAP both for "purified" and for "phosphate." If, however, each of these third-part abbreviations requires individual approval, no real difficulty should arise.

We should be extremely glad to have comments on these proposals.

We should like to acknowledge our debt to all the members of the Serological Products Committee of the British Pharmacopoeia Commission, and especially to Professor C. L. Oakley, for helpful criticism. We would also like to thank Mr. A. T. Glenny, F.R.S., who has given us detailed comments on many of our suggestions.

Internships Completed In Hospital Pharmacy - 1956

Several individuals completed programs of advance training and/or education in hospital pharmacy during 1956. Of the following list of 33 individuals, 20 received Certificates of Internship in Hospital Pharmacy, 12 were on a combined program and received a Master of Science degree from a college or university in addition to a Certificate of Internship from a hospital, and one individual with several years experience in hospital pharmacy received a Master of Science degree with a major in hospital pharmacy. Some institutions did not respond to the request for information. The following individuals are those, based upon the responses received, who completed internships and/or graduate study in hospital pharmacy during 1956:

BAKER, JOHN received a Certificate of Internship from the University Hospital, Ann Arbor, Michigan and a Master of Science degree from the University of Michigan in June 1956. Mr. Baker is now employed as Chief Pharmacist at Medical College Hospital, Medical College of South Carolina, Charleston, South Carolina.

BAYAS, JOSEPH G. received a Certificate of Internship from the Greenwich Hospital Association, Greenwich, Connecticut in 1956.

BAZEL, CHESTER received a Certificate of Internship from the Veterans Administration Center, Los Angeles, California and a Master of Science degree from the University of Southern California, Los Angeles, California. Mr. Bazel is now employed as Chief of Teaching Section at the Veterans Administration Center, Los Angeles.

BELLINO, ANGELUS received a Certificate of Internship from the Hackensack Hospital Association, Hospital Place, Hackensack, New Jersey in July 1956. Mr. Bellino is now employed as Chief Pharmacist at a nearby hospital in Northern New Jersey.

BORUQUE, MARIE received a Certificate of Internship from the University of Iowa Hospitals, Iowa City, Iowa, and a Master of Science degree from the State University of Iowa in June, 1956. Miss Boruque is now employed at the Cleveland Clinics, Cleveland, Ohio.

CARUSO, UGO F. received a Certificate of Internship from Jefferson Hospital, Philadelphia, Pennsylvania in May 1956. Mr. Caruso is now employed as Director of Pharmacy Service at the Grace-New Haven Community Hospital, New Haven, Connecticut.

CASENAS, LUCIA received a Certificate of Internship from the University of California Hospital, San Francisco, California and a Master of Science degree from the University of California, San Francisco 22, California in 1956.

COLLINS, EARL P. received a Certificate of Internship from Freedmen's Hospital, Washington, D. C. in June 1956. Mr. Collins is now employed as a pharmacist in a commercial store in Pittsburgh, Pennsylvania.

FISCHER, WALTER received a Certificate of Internship from the Veterans Administration Center in Los Angeles, California and a Master of Science degree from the University of Southern California, Los Angeles, California. Mr. Fischer is now employed as Staff Pharmacist at the University of California Medical Center, Los Angeles, California.

KABAT, HUGH received a Certificate of Internship from the University Hospital, Ann Arbor, Michigan and a Master of Science degree from the University of Michigan in June 1956. Mr. Kabat is now employed by the Public Health Service, Alaska Native Hospital, Mt. Edgecumbe, Alaska.

LACAPRIA, NANCY received a Certificate of Internship from St. Mary's Hospital, Brooklyn, New York in July 1956. Miss Lacapria is now employed at the Long Island Jewish Hospital, 270-05 76th Avenue, New Hyde Park, Long Island, New York.

LEDDA, LOURDES received a Certificate of Internship from Queen of Angels Hospital, 2301 Bellevue Avenue, Los Angeles, California in September 1956.

LING, FRANCES received a Certificate of Internship from St. Clare's Hospital, New York, New York in 1956. Miss Ling is now employed at St. Clare's Hospital, 415 W. 51st Street, New York 19, New York.

MASTRIANI, JOSEPH C. received a Certificate of Internship from The Johns Hopkins Hospital, Baltimore 5, Maryland and a Master of Science degree from the University of Maryland in June 1956. Mr. Mastriani is now with the Army.

MATSON, JERRY W. received a Certificate of Internship from the New Orleans Public Health Service Hospital, New Orleans, Louisiana in 1956.

MCCONNELL, ROBERT received a Certificate of Internship from University of Minnesota Hospital, Minneapolis 14, Minnesota in 1956.

MCCORMICK, SHIRLEY (Swinson) received a Certificate of Internship from the University Hospital, Ann Arbor, Michigan and a Master of Science degree from the University of Michigan in June 1956. Mrs. McCormick is now employed at the University Hospital, Ann Arbor, Michigan.

MCGREGOR, JANICE completed her internship requirements at the Lincoln General Hospital, Lincoln, Nebraska in July 1956 and will receive her Master of Science degree from the University of Nebraska, Lincoln, Nebraska and Certificate of Internship from Lincoln General Hospital in 1957. Mrs. McGregor is now employed at the Oak Park Hospital in Chicago, Illinois.

MCGREGOR, THOMAS DANIEL received a Certificate of Internship from the Madison General Hospital, Madison, Wisconsin in 1956. Mr. McGregor is now employed as general manager of three drug stores in Milwaukee, Wisconsin.

MILLER, LOWELL F. received a Certificate of Internship from Seattle Public Health Service Hospital, Seattle, Washington in 1956.

NEWELL, NANCY LUNDGREN received a Certificate of Internship from Madison General Hospital, Madison, Wisconsin in 1956. Mrs. Newell is now employed as a staff pharmacist at the Madison General Hospital.

OLYNYK, IRENE received a Master of Science degree with a major in Hospital Pharmacy from Purdue University, Lafayette, Indiana in January 1956. Miss Olynyk is now employed with Ayerst, McKenna and Harrison, Rouse's Point, New York.

PUFESCUE, DOINA received a Certificate of Internship from the University of Iowa Hospitals, Iowa City, Iowa, and a Master of Science degree from the State University of Iowa in June, 1956.. Miss Pufescue is now employed at the Mercy Hospital in Spokane, Washington.

RESARE, ROBERT received a Certificate of Internship from the Good Samaritan Hospital, Portland 10, Oregon in December 1956.

RUDY, WILLIAM KEITH received a Certificate of Internship from the Saginaw General Hospital, Saginaw, Michigan in February 1956. Mr. Rudy is now employed as a senior staff pharmacist at Saginaw General Hospital.

SAYOC, FRANCISCA T. received a Certificate of Internship from the Philadelphia General Hospital, Philadelphia, Pennsylvania in December 1956.

SCHWARTZ, SHELDON J. received a Certificate of Internship from Freedmen's Hospital, Washington, D. C. in June 1956.

SEMPOWSKI, HENRY received a Certificate of Internship from Mercy Hospital, Toledo, Ohio in September 1956. Mr. Sempowski is now employed as a Professional Relations Representative at the Rupp and Bowman Company, 319 Superior Street, Toledo, Ohio.

SISTER CECILIA MARIE received a Certificate of Internship from St. Mary's Group of Hospitals, St. Louis, Missouri and a Master of Science degree from the St. Louis College of Pharmacy and Allied Sciences, St. Louis, Missouri in June 1956. Sister Cecilia Marie is now employed at St. Mary's Group of Hospitals, St. Louis, Missouri.

SISTER MARY DAVID received a Certificate of Internship from St. Mary's Group of Hospitals, St. Louis, Missouri and a Master of Science degree from St. Louis College of Pharmacy and Allied Sciences, St. Louis, Missouri in June 1956. Sister Mary David is now employed at St. Mary's Group of Hospitals, St. Louis, Missouri

SISTER MARY GABRIEL, O.S.F. received a Certificate of Internship from Mercy Hospital, Toledo, Ohio in September 1956. Sister Mary Gabriel is now in charge of the Pharmacy Service at St. Mary's Hospital, 2400 E. Mitchell, Humbold, Tennessee.

TROSPER, EDITH received a Certificate of Internship from Duke Hospital, Durham, North Carolina on October 31, 1956. Miss Trosper is now working on the staff at Duke Hospital.

WESBURY, STUART A. received a Certificate of Internship from Baltimore Public Health Service Hospital, Baltimore, Maryland in 1956. Mr. Wesbury is now employed by the U. S. Public Health Service Hospital, Baltimore 11, Maryland.

PUBLIC RELATIONS AT WORK

Hospital pharmacists perform vital, behind-the-scenes jobs

OCTOBER 7 TO 13 IS NATIONAL PHARMACY WEEK allowing people everywhere to express special appreciation to the men and women of the pharmaceutical profession who are constantly doing their part in contributing to the advancement of better community health throughout the country.

When speaking of a pharmacist, one is prone to think of the kindly old gentleman at the corner drug store who has faithfully served the people of the neighborhood for a number of years. You are apt to think of this gentleman first, because you have personal over-the-counter contact with him from time to time.

There are many others in the pharmaceutical field whom you never meet face to face. The scientists, research specialists, laboratory technicians and medical writers are only a few. They remain behind the scenes, but the work they do opens roads to new horizons in the medical field.

Another unseen worker is the hospital pharmacist. Patients throughout the nation's hospitals receive their prescribed medications with regularity, but the administering of the prescriptions is generally handled by the nurses or other qualified persons.

In commemoration of National Pharmacy Week, Benjamin W. Wright, administrator of The Hospital Center at Orange, points with pride to the pharmaceutical facilities which serve Orange Memorial Hospital and New Jersey Orthopaedic Hospital, the two major units comprising The Hospital Center.

"The best way to describe our pharmacy," Mr. Wright said, "is to say that it a medicinal receiving station, warehouse and outlet through which numerous requests for medications are handled by a skilled staff of workers who go about their duties in an efficient and indefatigable manner.

Published as an example of a public relations program for hospital pharmacy during National Pharmacy Week, or other special occasion.

It's smiles all around as Mrs. Benedetta Giannotto, Newark retail pharmacist (seated left), Rudy Wilhelm, pharmacist at St. Michael's Hospital, Newark, Joseph Jasaitus, president of the Rutgers University College of Pharmacy Student Council, Raphael Taub, Newark professional pharmacist (standing left to right) and Dr. John L. Voigt, director of the New Jersey State University Pharmaceutical Extension Service, watch Mayor Leo P. Carlin of Newark (center) sign a National Pharmacy Week proclamation.

Their activities are carried on strictly behind the scenes, and I welcome this opportunity of National Pharmacy Week to pay tribute to them as well as all the pharmacists throughout the country."

A quick check of the records reveals why the pharmacy is such a busy place. During 1955, the Pharmacy at The Hospital Center prepared 3,284 new prescriptions and 926 refills for outpatients alone. In addition, this department handled 17,-381 special medications for inpatients at Orange Memorial Hospital. These figures do not include medications and prescriptions that were sent in bulk form to the New Jersey Orthopaedic Hospital, which is located two blocks away from the main buildings.

Heading the pharmacy staff at The Hospital Center is Mrs. Emma M. LaManna, a conscientious registered pharmacist who meets every request with confidence and an enthusiastic attitude.

A graduate of Rutgers College of Pharmacy in Newark, Mrs. LaManna joined The Hospital Center staff in February of 1951. In less than six years, she has developed and maintained the Pharmacy in such a way that it is one of the busiest and most efficient of any hospital pharmacy its size.

This current assignment is not the first time Mrs. LaManna has been directly associated with a hospital. From 1931 to 1945, she worked in the pharmacy at Christ Hospital in Jersey City. From 1945 until she accepted her job at the Orange institution, she undertook the duties of being a housewife.

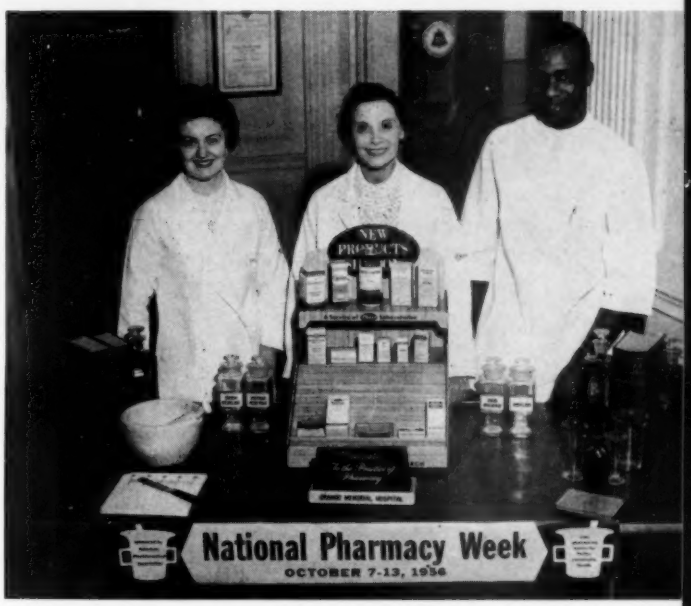
Even as a housewife, Mrs. LaManna was so dedicated to her profession that she often worked part-time in drug stores. Finally, she decided to return to full-time duties, and that is when she began her tenure at The Hospital Center. Mrs. LaManna holds membership in the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

In all, the Pharmacy is manned by two pharmacists, a pharmacist's assistant, and two part-time workers.

The other registered pharmacist is Miss Pauline Walsh, also a graduate of the Rutgers College of Pharmacy. Possessed with a fine personality and a charming smile, Miss Walsh has been a member of the staff since June of 1950.

The real veteran of the pharmacy in terms of service is Frederick Harris, the pharmacist's assistant, who has been employed at The Hospital Center for 17 years. Mrs. Eleanor Keeler and Raymond Holmes are the two part-time workers.

Mrs. LaManna conservatively estimates that The Hospital Center Pharmacy constantly stocks



Members of the Pharmacy Department staff at The Hospital Center at Orange, N. J., stand proudly behind the exhibit they displayed in the hospital lobby during National Pharmacy Week, October 7-13. Reading from left to right, the staff members are Miss Pauline Walsh, assistant pharmacist; Mrs. Emma M. LaManna, chief pharmacist, and Mr. Frederick Harris, pharmacist's assistant. Both Mrs. LaManna and Miss Walsh are registered pharmacists and graduates of the Rutgers College of Pharmacy in Newark, N. J.

1600 different items. These medications and ingredients include chemicals, cough mixtures, antacids, liniments, biologicals, antibiotics, hypnotics, narcotics, tonics, antihistamines, vitamins, and cathartics.

The narcotics, of course, are carefully controlled. They are kept locked in a large safe and are dispensed only by the pharmacists to the nurses. Before a nurse can obtain narcotics from the Pharmacy, she must present a prescription or request from the floor where she is working. Upon receiving the narcotics, the nurse must then sign for them and certify that she received the prescribed quantity.

Mrs. LaManna maintains a perpetual inventory of all narcotics and keeps a record of the quantity of each dose, the patient's name, and the name of the doctor prescribing the medication.

As you can see, hospital pharmacy operation is a large operation. The pharmaceutical profession is an exacting one, leaving no room for error. People often take the work of a hospital pharmacist for granted.

"We don't mind that," Mrs. LaManna explained. "After all, everybody's work around a hospital is important and exacting. Those of us in the Pharmacy are proud to be a part of the overall hospital team which constantly contributes to higher medical standards and better community health."

therapeutic TRENDS

edited by WILLIAM JOHNSON

Warfarin Sodium

Considerable experience has been accrued with the use of warfarin sodium administered orally and intravenously in anticoagulant therapy. However, there are occasions when it may be desirable to use another route of administration if feasible. Experience with rectal use of warfarin sodium in 23 patients has been reported by Freeman and Meyer in *Soc. Exptl. Biol. Med. Proc.* 92:52 (May) 1956. These workers report that warfarin sodium in a polyethylene glycol base as a rectal suppository is absorbed with sufficient regularity so that its use is a practical method for administering a coumarin anticoagulant to lower the prothrombin to therapeutic levels. It is of particular value, obviously, in the treatment of a patient who is incapable of taking oral medication. In contrast to Dicumarol, the rectal administration of warfarin sodium is consistently effective. If certain precautions are taken, the rectal route appears to be as reliable as the oral or intravenous, and in some circumstances it may be the route of choice. Warfarin sodium for this study was supplied by Endo Pharmaceutical Company as Coumadin.

Arlidin—A Vasodilator

Arlidin is (1-(p-hydrosyphenyl)-2-(l′-methyl-3′-phenyl amino) propanol hydrochloride). Pharmacologic and physiologic investigations indicated that Arlidin could be used with safety in humans, and that its chief peripheral effect was upon the vascular bed of exercising skeletal muscle. In *Ann. Internal Med.* 45:185 (August) 1956, Stein reports on the clinical evaluation of Arlidin after its use in two hundred twenty patients with intermittent claudication as the chief manifestation of a deficient blood supply to the working muscles of a limb. Their vascular insufficiency arose from organic arterial disease. It resulted in acute symptomatology in 20 patients, and slow development and gradual progression of symptoms in 199 patients. It was in this last mentioned group that the commonly used vasodilator drugs had little value in increasing the walking tolerance, after the initial salutary effect seen from the initial use of most new drugs. In contrast, when placed on oral Arlidin, two-thirds of these "stabilized" patients were able to demonstrate a significant increase in their ability to walk. Mention was made of the fact that intra-arterial injection of a single 6 mg. dose resulted in an average increase of blood-flow in the calf of 300 to 400 percent. Arlidin was supplied by the U. S. Vitamin Corp.

A Tumor-Inhibitory Substance

Submerged culture filtrates of a Streptomyces exhibited inhibitory activity toward a few bacteria and yeasts *in vitro*, a virus in embryonated eggs, mouse sarcoma 180 in mice, and C_3H mouse tumor in embryonated eggs. An agar-diffusion assay employing *T. albida* was established and used to measure antineoplastic activity. A typical fermentation is described. When biochemical and synthetic 6-diazo-5-oxo-L-norleucine (DON) became available, more extensive biologic tests were initiated. Of the 57 strains of bacteria tested, only 6 were sensitive 12.5 or less than 12.5 mcgm. DON/ml. The fungistatic effect of DON was tested *in vitro* on 104 strains of fungi. Only five yeasts were inhibited by 50 or less than 50 mcgm./ml. DON suppressed *Plasmodium lophurae* in chicks but only at toxic doses. DON was inactive as tested against *E. histolytica in vitro* and eight viruses in monkey kidney tissue culture at tolerated doses of 50 mcgm./ml. The acute intravenous LD_{50} for white mice was 76 mg./Kg. plus or minus 14 mg./Kg. DON is a fine, needle-like crystalline substance, light yellow-green in color, very soluble in water, and very sensitive to heat and *p*H, maximal stability at room temperature being at *p*H 5.0 to 6.0. This work was published in *Antibiot. and Chemotherap.* 6:487 (August) 1956 by Ehrlich *et al* of the research division of Parke Davis and Company.

Sulfamethoxypyridazine—A Long-Acting Sulfonamide

A new antibacterial sulfonamide, sulfamethoxypyridazine (3-sulfonamido-6-methoxypyridazine) was found to have the following properties, judged from experiments in dogs, rabbits, and mice: high solubility in urine, good absorption from the gastrointestinal tract, very slow urinary excretion,

poor acetylation, good penetration into the brain, and antibacterial activity equivalent to sulfadiazine. Nichols *et al* report the following observations in *Soc. Exptl. Biol. Med. Proc. 92*:637 (July) 1956 after giving a single dose of 4.0 Gm. of sulfamethoxypyridazine to 6 normal adult males. The drug was well absorbed, yielding high levels of free drug and only small amounts in acetylated form in the plasma. Little if any of the drug diffuses into the blood cells. The drug is cleared slowly from the plasma the acetylated form being cleared by the kidney about 11 times as fast as the free drug. Urine concentrations varied up to about 200 mg. percent, between 35 and 60 percent being in the conjugated form. Significant levels were still present in the blood and urine 105 hours after the dose. The only untoward effect experienced by 3 of the 6 subjects was some lassitude followed by frontal headache that began between 3 and 5 hours after the dose and lasted 4 or 5 hours. The headache was aggravated by sudden motions of the head but this did not interfere with normal activity. The drug for this study was supplied by Lederle Laboratories under the trade-name Kynex.

Test for Detection of PAS in Urine

Long-term PAS (para-aminosalicylic) therapy is now often prescribed for tuberculous outpatients in combination with either isoniazid or streptomycin. It is clearly important that the PAS be actually taken, because the tubercule bacilli may otherwise quickly become resistant to one of the other drugs when administered alone. Attention is drawn by Penman and Wraith in *Lancet II*:*552* (Sept. 15) 1956 to two simple tests to detect PAS in urine. In their experience they have found patients who had admitted that for various reasons they had temporarily omitted the drug. They suggest that if one or both of these tests are occasionally used in chest clinics, underhand perhaps though they seem, some interesting results will be forthcoming. The first test involves the drop by drop addition of 0.5 ml. of Ehrlich's reagent to 5 ml. of urine. PAS is detected by the immediate development of a lemon-yellow color. The color produced is not unlike that of urine, but these workers state that if the evening dose is taken it can be detected in the first urine passed the next morning. In the second test, 5 percent ferric chloride in 1 percent hydrochloride acid is added drop by drop to urine. The presence of PAS is indicated by a deep reddish-brown color which develops almost immediately. Urine from patients taking salicylates, aspirin, or in ketosis will give this same reaction but a negative test, however, would seem significant.

Prestonal—A Muscle Relaxant

Prestonal, dioxahexadekaniumbromide, is a colorless crystalline powder, easily soluble in water with a melting point of 146° C. An aqueous solution is practically neutral, but at a *p*H of 7.4 and 37° C., Prestonal is spontaneously decomposed by hydrolysis to an extent of 50 percent in 40 minutes. Solutions adjusted to a *p*H of 3.2 have been proven to be stable, even when stored for a considerable period of time. The J. R. Geigy Company has prepared the product Prestonal Geigy in a 1 percent solution with 100 mg. in each 10 ml. ampul. When 50 mg. of this solution of Prestonal are mixed in a syringe with 375 or 500 mg. of 2 percent or 3 percent thiopental respectively, a milky solution results. However, if this solution is left quietly on the table for a few minutes, it readily becomes clear and is satisfactory for use. According to a preliminary report of a clinical study of Prestonal by Griffith *et al* as published in *Can. Anaes. Soc. J. 3*:346 (October) 1956, the drug is capable of producing good relaxation of skeletal muscles. The duration of relaxation after a single dose is relatively short, probably between 6 and 8 minutes, but periods of relaxation up to 30 minutes may follow repeated doses or continuous infusion. The block appears to be of the mixed type, and thus antagonists are not convincing. The method of breakdown of the drug has not been established although hydrolysis by enzymes has been suggested. No serious undesirable side effects have been found thus far. Although much more experience is necessary to evaluate this drug, Prestonal has some advantages over the current popular relaxants.

Helenine—an Antiviral Agent

Crude preparations from two species of penicillium, *P. stoloniferum* and *P. funiculosum,* have been reported to be effective against certain small neurotropic viruses such as Semliki Forest, MM, and Columbia SK. Helenine is the antiviral agent obtained from *P. funiculosum,* and its effect on experimental poliomyelitis in mice and monkeys was investigated by Cochran and Francis. They report in *Soc. Exptl. Biol. Med. Proc. 92*:230 (May) 1956 that helenine was found to be an effective prophylactic against poliomyelitis in monkeys. In contrast to its effectiveness in monkeys, helenine did not alter significantly the incidence of paralysis in mice, although it did appear to prolong the incubation period. A species difference in the response of the host to this material seems unlikely in view of the effectiveness of helenine against other neurotropic viruses in mice.

timely drugs

Ataraxoid

. . . for rheumatoid arthritis, other collagen diseases, bronchial asthma, and inflammatory dermatoses, has been released by Pfizer Laboratories. Ataraxoid is a combination of Atarax (hydroxyzine) hydrochloride and Sterane (prednisolone, Pfizer) which permits simultaneous symptomatic control and reduction of attendant anxiety and apprehension in rheumatoid arthritis and other indications. Its anti-rheumatic, anti-inflammatory activity is 3 to 5 times that of hydrocortisone or cortisone. It is effective with a radically reduced steroid dosage as compared to the older steroids, and produces virtually no disturbance of electrolyte and fluid metabolism.

In severe rheumatoid arthritis the initial dose of Ataraxoid is 4 to 6 tablets daily; in less severe cases, 3 to 4 tablets daily. Good response is usually noted within three to seven days. Dosage is reduced gradually by ½ to 1 tablet every four or five days to obtain a maintenance dose, usually ranging between 1 and 4 tablets daily. Dosage is prescribed in divided doses, after meals and at bedtime. In other indications, usually 4 to 8 tablets daily is the initial dosage; then follow dosage schedule as previously outlined.

Each green, scored Ataraxoid tablet contains 5 mg. prednisolone and 10 mg. hydroxyzine hydrochloride, and is supplied in bottles of 30 and 100 tablets.

Eldec Kapseals

. . . a vitamin-mineral-hormone supplement for aid in the practice of preventive geriatrics, has been released by Parke, Davis & Co. Each capsule contains vitamins, minerals, digestive enzymes, protein factors, estrogen (Theelin), and androgen (methyltestosterone). It is designed to help ward off symptoms of aging by supplying vitamins and minerals to improve cellular function, enzymes to aid digestion, protein factors to help maintain nitrogen balance, and steroids to influence metabolism.

The usual daily dosage of Eldec is one capsule three times daily before meals. Female patients should follow each 21-day course with a 7-day rest interval. Eldec is available in bottles of 100 capsules.

Enemol

. . . a disposable general purpose enema used for emptying of the rectum and sigmoid colon, has recently been released by Cutter Laboratories. It is packaged in a polyethylene tube with a vinyl closure which seals off the contents of the tube until the patient is made ready. A variable size orifice in the closure is adjusted by rotating the container slightly until the rate of flow is satisfactory. The tube is then gently squeezed until contents are evacuated, at which time the tube is discarded. The 4½ fluidounce contents of the tube closely approximate the prescribed dosage for adults. Each 100 ml. of solution contains Sodium Biphosphate U.S.P. 16 Gm., Sodium Phosphate N.F. 6 Gm., Methylparaben 0.1 Gm., and Propylparaben 0.01 Gm.

Molofac Capsules

. . . a wetting agent (dioctyl sodium sulfosuccinate, Squibb) that effectively eases defecation by softening stools, has been announced by E. R. Squibb & Sons. Molofac lowers the surface tension of intestinal liquids so that they penetrate and permeate the fecal mass, thus producing softer stools for easier passage. It is particularly valuable for the prevention or relief of constipation in patients with hemorrhoids, anal fissure, megacolon, rectal abscesses, and allied conditions; pregnant and postpartum patients; patients scheduled for surgery; sedentary, elderly patients; cardiac and hypertensive patients; paralyzed patients and patients with muscle weakness.

Dosage of Molofac in mild constipation is 1 or 2 capsules daily for adults and older children; children 6 to 12 receive 1 capsule daily. In more severe constipation, an initial dose of 2 capsules twice daily for three days, with 1 or 2 capsules daily thereafter, is recommended for adults and older children. The stool softening effect of the drug is usually observed 1 to 3 days after the beginning of treatment. Molofac capsules are supplied in bottles of 30 and 100. Each clear, red capsule contains 60 mg. of the drug.

Paskate

. . . recently announced by Eli Lilly & Co., is an adjuvant in the treatment of tuberculosis. It is the potassium salt of aminosalicylic acid and is identical in therapeutic action with PAS or its sodium or calcium salts. However, it contains about 11 percent more PAS than sodium aminosalicylate and is the most soluble PAS salt known. Because of this greater solubility, blood concentrations reach a peak in one hour and are generally higher than those from comparable doses of other PAS forms. Renal excretion of the drug is rapid, being virtually complete in less than 12 hours.

Paskate is indicated as an adjunct to other antituberculous drugs such as isoniazid, streptomycin, and dihydrostreptomycin. It is also recommended in tuberculous patients who must be on a restricted sodium diet.

An adult patient should receive 12 grams daily in three or four divided doses by oral administration. Medication may be given without regard to meals.

Paskate is supplied as 0.5 Gm. capsules in packages of 250, 1000, and 5000 capsules.

Pyribenzamine Injectable Solution

. . . to prevent drug and blood transfusion reactions, is now supplied in multiple dose vials according to a New Product Bulletin of Ciba Pharmaceutical Products, Inc. Pyribenzamine (tripelennamine, Ciba) hydrochloride injection is also useful for rapid and prolonged relief of allergic symptoms in conditions such as urticaria, bronchial asthma, allergic rhinitis, dermatitis venenata, and serum and hyposensitization reactions.

Allergic and pyrogenic transfusion reactions can be greatly minimized, if not completely eliminated, by injecting 25 mg. (1 ml.) of Pyribenzamine injection through the air-vent needle directly into each bottle of blood to be transfused. When used to prevent penicillin or other drug reactions, 25 mg. of Pyribenzamine may be injected in the same syringe. (A list of compatible drugs may be obtained by writing to the Ciba Medical Service Division.) Administration can be intravenous or intramuscular. Intravenous administration should be made slowly with the patient in a recumbent position. If preferred, 25 mg. added to 200 ml. of normal saline can be given by intravenous drip over 1½ to 2 hours.

Pyribenzamine hydrochloride injection is packaged as 10 ml. vials with each ml. containing 25 mg. of the drug, in addition to the 1 ml. (25 mg.) ampuls formerly available.

Senokot Tablets

. . . developed from Cassia acutifolia (senna) pods, are available from the Purdue Frederick Co., and provide stable, gentle, large bowel neuro-peristaltic action without griping or rebound. They are intended for the treatment and correction of constipation. Unlike other purgatives or laxatives, Senokot aims for eventual freedom from all medication and is recommended as a safe remedy for children and adults suffering routine irregularity. Although the dosage varies with indications, usually one or two tablets before bedtime, or as directed, are recommended. Senokot tablets are supplied in bottles of 100.

Seromycin

. . . a new antibiotic produced by a strain of *Streptomyces orchidaceus*, has been marketed by Eli Lilly & Co. It is indicated in the treatment of severe pulmonary tuberculosis. At present its use should be restricted initially to hospitalized patients who cannot tolerate established agents or in whom the tubercle bacillus has become resistant to streptomycin, isoniazid, aminosalicylic acid, viomycin, pyrazinoic acid amide, or combinations of these drugs. Preliminary studies indicate that Seromycin (cycloserine, Lilly) in combination with isoniazid is more effective in controlling tuberculous infections than Seromycin alone. Clinical evidence so far shows that the drug alone is not indicated in the treatment of previously untreated cases of pulmonary tuberculosis, since toxic by-effects and emergence of resistant organisms may occur.

Since a relatively large portion of Seromycin is excreted in the urine, dosage should be reduced for patients with impaired renal function. The drug is effective by mouth and is currently administered only by this route. If used alone, the dosage of Seromycin for adults is 250 mg. twice daily at 12-hour intervals for two weeks. Blood concentrations below 25-30 mcg. per ml. without clinical signs of toxicity may be an indication for increase in dosage to 250 mg. every eight hours. When Seromycin c INH (isoniazid, Lilly) is used, a dosage of 500 mg. daily is believed adequate and at present should not be exceeded.

Seromycin is available as 250 mg. capsules in bottles of 40 and 500. Seromycin c INH is a combination of Seromycin 250 mg. and isoniazid 150 mg., and is also available in bottles of 40 and 500.

Serpasil Parenteral Solution

. . . a tranquilizer and antihypertensive, has been issued by Ciba Pharmaceutical Products, Inc. in a new multiple dose vial containing 2.5 mg. Serpasil (reserpine, Ciba) per ml. It is indicated in hypertensive crisis, toxemia of pregnancy, and acute glomerulonephritis. In psychiatric conditions it is used to quiet acutely disturbed, unruly, psychotic patients. For acute hypertension, the recommended dose of parenteral Serpasil is 2.5 mg. intramuscularly, to be repeated every 8 to 24 hours. In psychiatric emergencies, 5.0 to 10 mg. intramuscularly generally tranquilizes the patient. When used for neuropsychiatric patients, in conjunction with oral therapy, 2.5 to 5.0 mg. may be administered intramuscularly, while oral medication is started at 1.0 mg. twice daily.

Serpasil injection has been available as 2 ml. ampuls, each ml. containing 2.5 mg. of the drug. The new multiple dose vial also contains 2.5 mg. per ml. in 10 ml. vials.

Sigmamycin

. . . (oleandomycin tetracycline) is a new broad-spectrum antimicrobial combination containing two parts of tetracycline and one part of oleandomycin. For oral administration, Sigmamycin is supplied in capsule form. It is indicated primarily in the treatment of infections due to gram-positive bacteria, gram-negative bacteria, rickettsiae, large viruses, and protozoa. Conditions which may be treated with Sigmamycin include pneumonia (with or without bacteremia), other infections of respiratory tract and related structures, genitourinary infections, and surgical infections. Sigmamycin is a product of Chas. Pfizer & Co., Inc.

Vioform-Hydrocortisone Cream

. . . a nontoxic, practically nonsensitizing, water-soluble preparation for the relief of itching and inflammation and rapid healing in various dermatologic disorders, has recently been announced by Ciba Pharmaceutical Products, Inc. It contains Vioform (iodochlorhydroxyquin, Ciba) 3 percent and hydrocortisone (free alcohol) 1 percent in a water-washable base.

This cream is especially useful for eczematous eruptions in acute, subacute and chronic stages and for control of inflammation, erythema, local edema, scaling and pruritus. It is applied 3 or 4 times daily. Contact should be avoided with linen or clothing since the iodine content of Vioform may stain some materials. Vioform-Hydrocortisone Cream is available in 5 Gm. and 10 Gm. tubes.

BOOK REVIEWS

ACCIDENTAL POISONING IN CHILDHOOD, 1956. Written by Edward Press, M.D., M.P.H.; prepared by the Committee on Accident Prevention, American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill. 9" x 5½", 131 pages. Price $3.00.

Accidental Poisoning in Childhood is "a reference-guide to the chemical constituents of common household substances, together with treatment recommendations for their accidental ingestion by children." This book might be said to have had its beginning in 1950 when the American Academy of Pediatrics, recognizing the increasingly greater hazards of accidental poisoning in children, formed a committee on Accident Prevention. From this committee developed, in 1953, the nation's first Poison Control Center. A summary of available literature on the chemical constituents of various household materials and the most recent, approved methods of treatment, was compiled by Dr. Press and circulated to Academy members and others. This summary, modified by revisions and suggestions of those using it in over a dozen Poison Control Centers and in scores of hospitals, forms the text of this book.

The number of potentially toxic substances in the home which may be accidentally swallowed by children is enormous. In 1954 nearly one-third of the 1,400 fatal home poisoning cases were from the 0 to 4 age group. The A.M.A. Committee on Toxicology estimates that there are over 250,000 different trade-name substances on the market today. Since no physician or pharmacist could possibly know the toxic constituents in all of these, it is obvious that a book of this nature is greatly needed. In fact, until Poison Control Centers become more numerous and familiar to those in the health professions as well as to laymen, many books such as this will be needed to list even a small portion of those 250,000 products.

This book is divided into three major sections, each with different colored pages for quick reference. Section I is devoted to types of treatment including first aid measures, general therapy, dosage of drugs and description of therapeutic measures, and toxicological analysis and collection of laboratory specimens. Section II consists of a list of toxic substances and suggested treatment. In this table many entries under "Suggested Treatment" state "See ricin," or "See aconotine"; other entries indicate only a name of a drug or procedure for treatment with a page reference to section I. Although the reference is generally sufficient when found, this method does involve considerable page-flipping, further complicated often by the reader's sense of urgency in actual cases of poisoning.

Section III contains the toxic constituents of household products including drugs, cosmetic and toilet goods, pesticides, cleansing, polishing and sanitizing agents, and poisonous plants. A separate table lists insecticides identified by letters or numbers. According to the text, this section was "compiled by enumerating most of the substances that were reported through the Chicago Poison Control Center and several other centers . . ." Obviously, no one table can begin to include all substances which may cause poisoning and about which pharmacists may be called for information. However, two omissions were found immediately by one pharmacist when the ingredients were requested for Bromo-Seltzer and Ronsonol lighter fluid. This is not necessarily a criticism of the book; it merely points out the need for several such books in the pharmacy. There cannot be too many references available when a poisoning occurs. The American Academy of Pediatrics is to be commended for its efforts in making Accidental Poisoning in Childhood available. The American Medical Association, The AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, and other organizations in the health field should be encouraged to compile and distribute similar texts.

Joanne Branson

MEDICAL PARASITOLOGY Second Edition 1956. By William G. Sawitz, M.D. Published by The Blakiston Division, McGraw-Hill Book Co, Inc., New York, N.Y. 9¼" x 6¼", 342 pages. Price $6.00

Medical Parasitology is a text intended for medical students and practicing physicians. It contains excellent discussions of the various types of protozoa, helminths, and arthropoda which produce disease in man. Helpful information on the incidence and prevalence of diseases caused by parasites is given. The life cycle and identifying characteristics of the parasites are discussed. This section of the book is well illustrated with numerous, clearly drawn illustrations which add considerable value to the book.

Of special interest to hospital pharmacists is the chapter devoted to the treatment of conditions produced by infection or infestation with protozoa, helminths, and arthropoda. In this chapter, the individual drugs are discussed under the headings of preparations, dosage, efficacy, toxicity, and contraindications. In addition, this chapter contains a section devoted to insecticides, with emphasis on their toxicity. In some cases, general suggestions for treatment of poisoning by insecticides are given.

Medical Parasitology is a useful reference book especially to those hospital pharmacists who teach student nurses. The chapter on the treatment of the various conditions caused by parasites makes it a helpful reference tool for departmental use when brief, concise information is wanted rapidly.

DON E. FRANCKE

ASHP affiliates

Midwest Association

The regular meeting of the Midwest Association of Sister Pharmacists was held at St. Elizabeth Hospital, Danville, Illinois, on September 20, 1956.

The principal speaker, Dr. H. Klschuer, presented an interesting discussion on degenerating diseases and their effect on the circulatory system, along with slides showing the different clinical cases of diseases of the blood system. Sister M. Vincentiana presented a paper on "The Latest on Narcotics in Hospitals," and Sister M. Grace spoke on "Pharmacy Law".

The following new officers* for 1956-57 were announced: *President,* Sister Hortensis, St. Elizabeth Hospital, Chicago; *Vice-President,* Sister Cherubim, St. Joseph Hospital, Joliet; *Treasurer,* Sister Theodore, St. Elizabeth Hospital, Danville, Illinois; and *Secretary,* Sister Anne Gallagher, St. Bernard Hospital, Chicago.

A one day Institute to be held on December 6th at the University of Wisconsin in Madison was announced by Sister Cherubim. Plans were made for the November meeting to take place at the same time. Sister Josita invited the Sisters to Chicago Heights to St. James Hospital for the February 1957 meeting.

Rhode Island Society

Members of the Rhode Island Society of Hospital Pharmacists are launching a campaign to interest all hospital pharmacists in the state in both the national and local groups. Mr. Victor Canaipi has been appointed to represent the Rhode Island Society on the Membership Committee of the national organization.

The Annual Meeting of the Rhode Island Society was held on Friday, September 21 at Johnson's Hummocks with 20 members present. During the business session consideration was given to interesting students in the Rhode Island Society and general attention was given to planning better programs. President Gilberti announced plans for the program for the New England Council of Hospital Pharmacists which will hold a Seminar on October 30 and 31 at the Hotel Sheraton in Hartford, Connecticut.

New officers* of the Rhode Island Society elected at the September meeting include: *President,* Edward Gilberti, State Hospital, Howard, R. I.; *Vice-President,* Joseph Giardino, Roger Williams General Hospital, Providence, R. I.; and *Secretary,* Victor Canaipi, Zambarano Memorial Hospital Wallum Lake, R. I. Other members of the Executive Committee include: Anthony Longo, Lucille Jabbour, Joseph H. Procopio, Frank Chase, and John McCormick.

The program for the September meeting included a film on nystatin made available by the E. R. Squibb Company.

Greater St. Louis Association

The Hospital Pharmacists' Association of Greater St. Louis met in the lobby of the new Cardinal Glennon Memorial Hospital for Children, Tuesday evening, September 11 at 7:00 P.M. The members and guests were divided into small groups for a tour of the hospital with the Sisters of St. Mary acting as guides. All were impressed with the magnificent facilities available for the care of child patients. Especially interesting to the group was the beautiful pharmacy with modern equipment for both dispensing

At 8:00 P.M. Schering Corporation served a delicious buffet supper in the hospital cafeteria to 21 members and 19 guests.

The meeting was called to order at 9:00 P.M. in the hospital cafeteria. Vice-President Joseph Guller presided in the absence of Mrs. Florence Mueller who was on vacation. The Minutes of the past meeting were read, corrected and approved. The Treasurer's report, prepared by Sister Mary David, was read by the Secretary. Mr. Guller then announced that the next meeting would be held at Christian Hospital, Tuesday evening, October 9.

Tentative plans were made for a one-day Seminar to be sponsored by the Pfizer Laboratories in cooperation with the Hospital Pharmacists' Association of Greater St. Louis. Appointed to serve on the program committee were Mr. Emmett H. Skinner, *Chairman,* Mrs. Florence Mueller, Sister Mary David, Mr. John Murphy, Mr. Armand Dellande, Mr. Joseph Guller, Mr. Norman Hammelman, Mr. Raymond Dye and Mr. Ned E. Kinney.

Dr. C. L. Huyck of the St. Louis College of Pharmacy also invited the members of the Greater St. Louis Association to attend a meeting of the St. Louis Branch of the American Pharmaceutical Association on October 3. Mr. J. Leo McMann, Editor of the *Midwest Druggist,* was to be the principal speaker.

Nebraska Society

The Annual Convention of the Nebraska Society of Hospital Pharmacists was held jointly with the Nebraska Hospital Association in Omaha on October 25 and 26. The meeting opened on Thursday evening with a banquet and a guest speaker, Frank Forgarty, Vice-

*New officers as listed here not included in green sheets of July August issue of THE BULLETIN.

President, Meredith Broadcasting Company. His subject was "Public Relations—What Does the Public Have to Say."

Papers presented during the one day session on Friday were as follows:

"You Are Your Own Worst Enemy," John A. Aita, M.D., Associate Professor of Neurology and Psychiatry, University of Nebraska, College of Medicine.

"Delayed-Action Drugs," (radioisotopes, hormones, etc.) D. Russell Zimmerman, New York, N.Y., Sales Manager, Special Products, E. R. Squibb & Sons.

"Modern Formulations," George L. Phillips, Assistant Chief Pharmacist, University Hospital, Ann Arbor, Michigan.

"Drugs Available for Mental Health Today," Elmer H. Funk, Jr., M. D., Medical Research Department, Wyeth & Company, Radnor, Pa.

Included also on the program was a tour of the new Bishop Clarkson Memorial Hospital where Mrs. Frances Rodgers, Chairman of the Program Committee, is Chief Pharmacist.

Michigan Society

"The Merits of Pharmacy and Therapeutics Committee," was the subject presented at the September 14 meeting of the Michigan Society of Hospital Pharmacists. The speaker was Dr. Latamer from the William Beaumont Hospital in Detroit.

The business session was called to order by President Don Melcher, who announced the new committee members for the current year. Mr. Duane Pavey, Chairman of the Entertainment Committee, announced plans for future meetings. Business covered during the session included election of a new Recording Secretary, Mrs. Patricia Allen, and a discussion of a proposed change in the Constitution calling for dues to be paid on the fiscal year basis, rather than by the calendar year.

Greater Kansas City Society

The Society of Hospital Pharmacists of Greater Kansas City met at St. Joseph's Hospital on September 11 at 2:00 P.M. The meeting was called to order by Mr. Charles Loomis, President, with 12 members present.

During the business session, plans were outlined for the Pharmacy Section Meeting to be held at the 1957 Convention of the Midwest Hospital Association. Arrangements were made to notify all hospital pharmacists in the area regarding the meeting and also to invite members of other ASHP chapters in the Midwest.

Mr. Loomis and Mr. Chipman reported on the Hospital Pharmacy Institute which was held in Chicago in August and suggested that consideration be given to holding an institute in Kansas City at some future date.

There was also some discusssion regarding the possibility of giving assistance to the University of Kansas City, in connection with a course in hospital pharmacy.

North Carolina Society

Mr. Grover C. Bowles, a Past President of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, was the speaker at the October 6 meeting of the North Carolina Society of Hospital Pharmacists. Included also on the program was a dinner sponsored by E. R. Squibb and Sons with an address by Dr. Paul Numerof on "Radio Isotopes."

The meeting was held at the Cabarrus Memorial Hospital in Concord, North Carolina.

Georgia Society

The Georgia Society of Hospital Pharmacists met on October 13 at the Goodrich Hotel in Sandersville, Georgia. New officers elected for the coming year include *President*, Douglas Johnson; *Vice-President*, Sarah Francis Reid; *Secretary*, Clara Greene; and *Treasurer*, W. S. Havron.

Western Pennsylvania Society

The Second Seminar on Hospital Pharmacy conducted by the Western Pennsylvania Society of Hospital Pharmacists with sponsorship by the Western Pennsylvania Hospital Council was held in Pittsburgh on October 18th. Meetings were held at the Veterans Administration Hospital and the Mercy Hospital with members of the Western Pennsylvania Society assisting with arrangements. Attendance reached that of the first seminar which was held in 1955, but it is reported that the crowd was more enthusiastic and local pharmacists in

Pittsburgh Seminar Participants and Committee—STANDING, LEFT TO RIGHT: *Italo Bianculli, James Sandala, Joseph A. Oddis, Dr. Joseph D. McEvilla, George L. Phillips, and Gerald Wolf;* SEATED, LEFT TO RIGHT: *Clifton Latiolais, Dr. George Archambault, Anne Keane, Josephine Certo, Sister M. Gonzales, and Dr. J. M. Josephs.*

greater numbers participated. Of particular note were the special guests attending, including hospital administrators, medical record librarians, pharmacy students from the two universities in Pittsburgh, nurses and neighboring hospital pharmacists from Ohio and New York.

Program participants from out of town included, Mr. Clifton J. Latiolais, Assistant Program Director, Audit of Pharmaceutical Service in Hospitals (A.Ph.A. and ASHP), Ann Arbor, Mich.; Mr. George Phillips, Assistant Chief Pharmacist, University Hospital, Ann Arbor, Mich.; Dr. J. M. Josephs, Director of the Biological Research Institute, Toledo, Ohio; Dr. George F. Archambault, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospital, U.S. Public Health Service, Washington, D. C.; and Mr. Joseph A. Oddis, Staff Representative, Council on Professional Practice, American Hospital Association, Chicago, Illinois. Also participating were Rev. Jerome Chintz, Catholic Chaplain, Veterans Administration Hospital, Pittsburgh, Pa.; Dr. Lee G. Sewall, Manager, Veterans Administration Hospital, Leech Farm Road, Pittsburgh, Pa.; Dr. Joseph D. McEvilla, Assistant Professor of Pharmacy Administration, School of Pharmacy, University of Pittsburgh, Pittsburgh, Pa.; Dr. John G. Adams, Dean, School of Pharmacy, Duquesne University, Pittsburgh, Pennsylvania.

A highlight of the program was a "Clinic on Hospital Pharmacy Problems," which was moderated by Mr. Joseph A. Oddis at the evening session. The program participants for the day served on the panel.

Michigan Society

Members of the Michigan Society of Hospital Pharmacists met at Mt. Carmel Hospital in Detroit on October 11. During the business session a report was received on plans for a joint meeting of the Detroit Retail Druggists' Association, the State Board of Pharmacy, and the Michigan Society of Hospital Pharmacists which is to be held in February, 1957. Also, it was voted to present the 1957 H.A.K. Whitney Award at the Annual Meeting of the national organization which is to be held in New York City in April. Further plans for developing the program are to be worked out at a later date in cooperation with the SOCIETY'S Executive Committee.

The program included a panel discussion on the advisability and advantages of displays in hospitals.

Arizona Society

The Arizona Society of Hospital Pharmacists met at the Pinal General Hospital in Florence on October 16. During the business session, plans were made for participation in National Pharmacy Week, presentation of a report on amendments to the Constitution and By-Laws and consideration of the possibility of participating in the Pharmacy Section of the Association of Western Hospitals. It was also announced that President of the national organization, Mr. Paul Parker, will be present for a dinner meeting early in October.

Oregon Society

Dr. Elmer Plein, Professor of Pharmacy from the University of Washington, was the guest speaker for the September 27 meeting of the Hospital Pharmacists of the State of Oregon. Dr. Plein's subject was "The Responsibilities of the Pharmacy." The meeting was held jointly with the Oregon Branch of the American Pharmaceutical Association at the Campbell Court Hotel in Portland.

Virginia Society

Plans have been outlined for the Virginia Society of Hospital Pharmacists to participate in the forthcoming meeting of the Virginia Hospital Association. It is anticipated that hospital pharmacists will participate in a joint meeting with administrators.

Philadelphia Hospital Pharmacists

Mr. Herbert L. Flack, President of the Philadelphia Hospital Pharmacists' Association, has issued a letter to the membership asking them to indicate their choices in committee work and other activities in the Society. Of particular note is the fact that the Philadelphia Association has 13 working committees participating throughout the year.

Northeastern New York Society

Mr. Louis P. Jeffrey, President of the Northeastern New York Society of Hospital Pharmacists, has outlined plans for the current year and made committee appointments. Serving as chairman will be the following: *Membership,* Benjamin Teplitsky; *Finance,* Louis P. Jeffrey; *By-Laws,* Lucy Manvel; *Program and Workshop,* Fay Peck Jr.; and *Publications,* Virginia McBride. Other members of the Executive Committee for the current year include the officers, Josephine Stancampiano and Violet Spaulding.

An outstanding meeting of the year for the members of the Northeastern New York Society was the Testimonial Dinner honoring Past President, Mr. Benjamin Teplitsky, on September 22. The dinner was held at the Sheraton Ten Eyck Hotel in Albany. Principal speakers included Dr. Ralph Metheny, Manager, Veterans Administration Hospital, Albany, New York, and President Paul Parker, of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. Also present were Mr. Dan Murphee, Central Office, Veterans Administration, Washington, D.C., and Mr. Charles W. Gill, Hospital Field Supervisor, Pfizer Laboratories. The toastmaster for the dinner was Mr. Irving Rubin, Managing Editor on Pharmacy of *American Druggist.* Speakers praised Mr. Teplitsky for his outstanding contributions to hospital pharmacy practice and his efforts as a leader in the Northeastern New York Society.

A forum discussion on "The Value of a Hospital Formulary," was held at the October 18 meeting of the Northeastern New York Society. Participants included a hospital administrator, Dr. Ferdinand Haase, Jr., Medical Director of Albany Hospital; a physician, Dr. Paul R. Patterson, Chairman of the Department of Pediatrics, Albany Medical College; a manufacturer, Mr. Vincent Coniglio, District Manager of Parke, Davis and Company; and an educator, Dr. Francis J. O'Brien, Dean of the Albany College of Pharmacy. The moderator was Mr. Louis P. Jeffrey, President. An exhibit of several formularies from outstanding hospitals in the country was also on display during the meeting.

as the president sees it

PAUL PARKER

American Pharmaceutical Association, Washington, D. C.

I am most appreciative of the hospitality which has been accorded me upon visiting so many of the Affiliated Chapters. It is encouraging to observe your Chapter activity; to know that the groups are giving attention to increasing our membership and to see the number who have enough interest in the organization to attend meetings and seminars regularly. It is particularly gratifying to see the progress that is being made to make hospital pharmacy service more valuable.

Though there are apparently many hospitals in which the pharmacy is expected to do no more than fill drug orders, still there are a great many hospital pharmacists who provide a very extensive professional service in their hospitals. These professional services are very apparent as one has the opportunity to visit with administrators, nursing directors, the staff physicians and others in the hospitals.

Our pressing problem is to improve the quality of hospital pharmacy practice in more and more hospitals. To make our services more valuable would do much to correct such other problems as poor pay, insufficient personnel, inadequate space, improper facilities and other needs which can too easily become the focus of our attention.

Your national organization has made great strides in recent years in establishing minimum standards and achieving their approval by other health organizations. Now we must think in terms of implementing these standards, which can only be done at the local level and in the individual hospitals. We must depend upon you, the individual hospital pharmacist to make these improvements and encourage and assist others in your area to do likewise.

Though the truly professional services may seem commonplace and trivial to those who provide them, it would no doubt be valuable to some if specific services could be discussed by local people in the meetings of the affiliated Chapters. The president of the Virginia Society, Mr. R. David Anderson, recently told me that essentially all the programs of their chapter were presented by their own members. Sometimes papers are read by local members which have been printed in THE BULLETIN even as much as four or five years ago. It would seem that this Chapter is vitally concerned about providing selected material which can be used in the hospitals represented by that group. Your Chapter of the ASHP can be the means by which ideas and information may be obtained from others and also a medium for passing along suggestions to help other hospital pharmacists make their services more valuable.

I have also been amazed in talking to the officers of local hospital associations at their eagerness to work with our local hospital pharmacy associations. Though some pharmacists may have the ability and desire to improve their services, they must also have the opportunity to do so. Frequently, the hospital administrator can help to provide this opportunity if he fully understands your motive.

Coodinating your Chapter activities wtih your State Hospital Association to explore the need and opportunities for better pharmaceutical services approaches the subject in a constructive and objective manner. We hope that such cooperative effort may achieve a greater understanding of the need for good pharmacy service in promoting better patient care.

Paul F. Parker

NEWS

Pan-American Congress of Pharmacy and Biochemistry

Robert A. Hardt

The Fourth Pan-American Congress of Pharmacy and Biochemistry will meet in Washington, D. C. the week of November 3, 1957. The Mayflower Hotel will serve as headquarters.

Chairman of the Organizing Committee for the Congress is Dr. Robert A. Hardt, Vice-President of Hoffmann-La Roche, Inc. Serving as Vice Chairman is Dr. Newell Stewart, Executive Vice-President of the National Pharmaceutical Council. Mr. George Griffenhagen, Acting Curator, Division of Medicine and Public Health of the Smithsonian Institution has been appointed Executive Secretary of the Congress. Mr. S. Barksdale Penick, Jr., President of the S. B. Penick and Company will serve as Treasurer, while Mr. Oscar A. Zeitz will be the Assistant Treasurer. Mr. Zeitz is the Assistant Treasurer and Controller of Hoffmann-La Roche. Dr. Hardt has appointed several committees to aid him in planning for the Congress.

The theme for the Congress will be "Planning the Advancement of Pharmacy throughout the Americas." The Congress will be dedicated to the advancement of pharmacy by fostering: Uniformly High Educational Standards, Greater Uniformity in Drug Standards and Regulations, and Prompt Availability of Therapeutic Agents. The Congress will stress the role of pharmacy in improving the public health in all the Americas. Problems fundamental to better public health will be discussed by eminent leaders in pharmacy and allied sciences. The subjects selected will show the progress in the education of practitioners of pharmacy, the need for uniform drug standards and regulations, and the necessity for facilitation of the prompt introduction of new therapeutic advances for the treatment of the sick of all countries. The Congress will offer a unique opportunity for interchange of ideas and cooperative action in the advancement of pharmacy as a profession throughout the Americas.

Hospital Pharmacists Participate in AHA Convention

More than twelve thousand hospital leaders from the United States and Canada attended the 1956 Convention of the American Hospital Association which was held in Chicago September, 15-18. The General Sessions and Round Table Discussions covering various phases of hospital practice followed the theme "Planning for the Future." The Division of Hospital Pharmacy, including the A.Ph.A. and the ASHP, was represented by a number of leaders in the field and an exhibit was sponsored by the Division. Mr. Paul Parker, President of the ASHP and Director of the Division, was present throughout the week.

One of the round table discussions on "New Developments in Hospital Pharmacy," offered an opportunity to bring to pharmacists and administrators reports on work being carried out in our specialty. With Dr. Robert R. Cadmus, Director of the North Carolina Memorial Hospital, as Chairman, participants included Dr. George F. Archambault, Pharmacist Director, Chief, Pharmacy Branch, Division of Hospitals, U. S. Public Health Service, Washington, D. C., and Dr. Don E. Francke, Chief Pharmacist, University Hospital, Ann Arbor, Michigan. In Dr. Archambault's discussion he covered the need for adequate staffing and the proper utilization of nonprofessional personnel in pharmacy, consideration of what constitutes adequate professional staffing for a hospital pharmacy, proper supervision and controls relative to the use of investigational drugs, the automatic stop-order on dangerous drugs, perpetual inventory control of amphetamines at nursing stations and medication centers the duplication-substitution problem, and disposable equipment affecting pharmacy practice. Dr. Francke covered the formulary system, pointing out the advantages and the philosophy of such a plan, the pharmacy committee, the current status of hospital pharmacy internships, and work on the Audit of Administrative and Professional Pharmaceutical Service in Hospitals.

Another hospital pharmacist participating in one of the round table sessions was Mr. Louis Gdalman, Director of Pharmacy at St. Luke's Hospital in Chicago. Mr. Gdalman participated in the round table session on "Training in Leadership."

1957 Texas Seminar Scheduled

The Ninth Annual Seminar for Hospital Pharmacists is scheduled for Saturday and Sunday, January 26 and 27, at the University of Texas in Austin. The Seminar will again be sponsored by the University of Texas College of Pharmacy, in cooperation with the Division of Extension. The Texas Society of Hospital Pharmacists will cooperate in connection with program arrangements through its Committee on Program and Public Relations, which is headed by Fred Borth of Austin. Other members of the committee include James Beran of Dallas and Cedric Jeffers of Temple.

Reporting of Adverse Reactions to Drugs

The Second Conference on the Reporting of Adverse Reactions to Drugs was held in Washington, D. C. on September 21. Sponsored by the Food and Drug Administration, the joint study is being developed in collaboration with the American Association of Medical Record Librarians, the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS, The American Medical Association, and the American Hospital Association. Dr. George F. Archambault, a past president of the ASHP, represented the SOCIETY at the October meeting and presented a statement on behalf of hospital pharmacists and their roles in reporting drug reactions.

The joint study has been undertaken on a pilot basis in eleven hospitals in the country. The purpose of the overall program is to obtain information regarding effects of drugs which may appear in some patients when they are administered to large numbers of people. This problem has been magnified by the increasing number of potent new drugs and it has been pointed out that even with the most extensive clinical studies, clinicians cannot always forecast all types of drug reactions which may develop throughout the population. In view of the fact that hospitals provide an ideal site for observing the effect of drugs and obtaining essential information, the Food and Drug Administration has set up the program in collaboration with the hospital and medical groups. Further details from the standpoint of pharmacists' interests are included in an article entitled "Reporting Drug Reactions," by Dr. Irvin Kerlan which appeared in the July-August (1956) issue of THE BULLETIN.

In Dr. Archambault's statement at the October Conference, he pointed out the interest of the

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Society and the need for cooperation with hospital pharmacists in developing the total program. He also reported on action taken by the Society regarding the program on recording and reporting adverse drug reaction and discussed with the members of the Conference the reaction of individual pharmacists to the procedure which has been developed. He urged that attention be given to further implementing the program and assured assistance from the American Society of Hospital Pharmacists in carrying out the study.

Three Million Prescriptions Filled Since 1930

Baylor Progress, publication from Baylor University Hospital in Dallas, Texas, reports that the Pharmacy Department filled its three millionth prescription on August 11, 1956. One million of these have been filled since 1952. Although Mr. Lewis Smith, Chief Pharmacist, was vacationing at the time, Pharmacists Charles Henry, Archie L. Webb, Jr., and Ray M. Costolow were present.

Film on Treatment of Moniliasis Available

The E. R. Squibb Company has announced the availability of a film entitled, "The Treatment of Moniliasis with Nystatin." Case studies—photographed in color—of a wide variety of typical moniliasis infections, their treatment and results of the treatment are presented.

Of interest to anyone concerned with the treatment of monilial infections, the film demonstrates nystatin's effective control of various manifestations of moniliasis through the presentation of cases at successive stages of diagnosis and treatment. These cases include oral thrush, diaper rash, monilian infections of the folds of the skin in various areas such as the groin, the umbilical area and the interdigital spaces.

The relation of broad-spectrum antibiotic therapy to monilial overgrowth is also discussed. Several examples of vaginal moniliasis, a common form of candida overgrowth, are shown before and after treatment with nystatin.

In full color with sound, the 16 mm. film "The Treatment of Moniliasis with Nystatin" runs for 20 minutes and is obtainable without charge for use by medical groups from Squibb, 745 Fifth Avenue, New York 22, N. Y.

Masur and Cronin Promoted

Dr. Leroy E. Burney, Surgeon General of the Public Health Service, has announced reassignment of Dr. Jack Masur, Chief of the Bureau of Medical Services, and Dr. John W. Cronin, Chief of the Hospital and Medical Survey and Construction Program. Dr. Masur will become Direc-

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tor of the Clinical Center at the National Institutes of Health in Bethesda, Maryland. Dr. John Cronin will become Chief of the Bureau of Medical Services which is in charge of administering the Public Health Service hospitals, the Hospital and Medical Facilities Survey and Construction Program, the Indian Health Program, the Foreign Quarantine Program, and the Dental and Nursing resources activities.

Dr. Vane M. Hoge, in addition to his duties as Associate Chief of the Bureau of Medical Services, will assume directorship of the Hospital and Medical Survey and Construction Program.

U.S.P. Reference Standards

A new booklet on U.S.P. Reference Standards, which supplements the one published in 1952, has recently been made available. The following new reference standards are described: Bacitracin, Chloramphenicol, Chlortetracycline Hydrochloride, Corticotropin (ACTH), Cortisone Acetate, Cyanocobalamin (Vitamin B_{12}), Dienestrol, Dihydrostreptomycin Sulfate, Erythromycin, Growth Hormone, Hyaluronidase, Hydrocortisone, Hydrocortisone Acetate, Neomycin Sulfate, Oxytetracycline, Polymyxin B Sulfate, Reserpine, Streptomycin Sulfate, Sulfadiazine, Sulfamerazine, Sulfamethazine, Tetracycline Hydrochloride, Thyrotropin, Vitamin A. A total of 68 U.S.P. Reference Standards are now available for purchase. Most packages contain sufficient material for at least ten to twenty assays. Three sets of U.S.P. Steroid Reference Substances are also available. The two booklets describing the reference standards may be obtained by addressing U.S.P. Reference Standards, 46 Park Avenue, New York 16, New York. The Reference Standards may also be ordered from the same source.

NWDA Drug Market Data Booklet

A booklet which gives the county by county tabulation of families, number of drug stores, and drug store sales 1954 compared with 1948, was published in June, 1956. The distribution map of the U.S. delineates 37 primary areas of influence by wholesale drug houses. The booklet is

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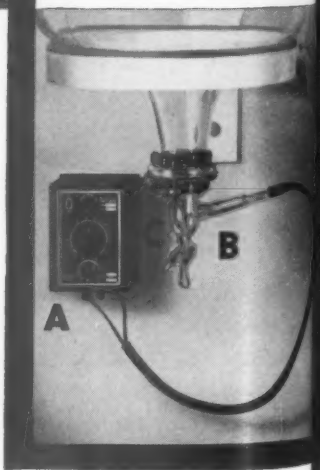

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A. C. A. Prescription Pharmacy Booklet

A booklet entitled *Facts on the Operation of Prescription Pharmacies 1955* is the fourth survey of operating costs of prescription departments made by the American College of Apothecaries. Based on returns from 89 pharmacies, the data includes information on: sales, cost of goods sold, gross profits, operating expenses, net before taxes, operating costs as function of prescription volume, and average operating costs. Some of the data is broken down by pharmacies with more than 50 percent of their volume from prescriptions, and those with less than 50 percent. The booklet includes tables, charts, and a discussion of the data. The booklet is available from the American College of Apothecaries, 39th and Chestnut Streets, Philadelphia 4, Pa., at a cost of 20 cents per copy. The booklet contains 10 pages.

Pfizer Sponsors Seminars

Pfizer Laboratories has recently sponsored a number of hospital pharmacy seminars in cooperation with local affiliated chapters of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. Among those sponsored recently have been the following:

October 6—Buffalo, N. Y. (in cooperation with the University of Buffalo School of Pharmacy and the Buffalo Chapter of the ASHP).

November 9—Philadelphia, Pa. (in cooperation with the Philadelphia Hospital Pharmacists' Association).

December 1—Cleveland, Ohio (in cooperation with the Cleveland Society of Hospital Pharmacists).

December 6—Madison, Wis. (in cooperation with the Wisconsin Society of Hospital Pharmacists).

December 8—St. Louis, Mo. (in cooperation with the Hospital Pharmacists' Association of Greater St. Louis).

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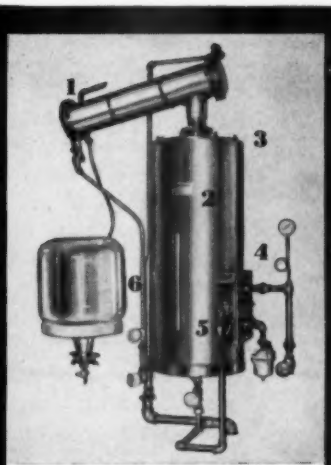

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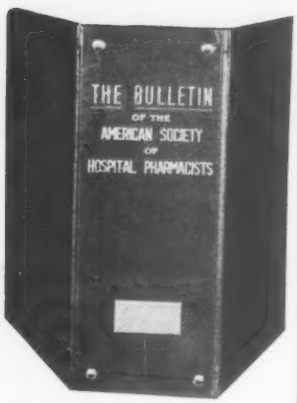

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